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(71) Applicant *(for all designated States except US)*: **ABGENIX, INC.** [US/US]; 6701 Kaiser Drive, Fremont, CA 94555 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **CORVALAN, Jose, R., F.** [CL/US]; 125 Williams Street, Foster City, CA 94404 (US). **JIA, Xiao-Chi** [US/US]; 22 Murray Court, San Mateo, CA 94403 (US). **FENG, Xiao** [US/US]; 135 Red Cedar Lane, Union City, CA 94587 (US). **YANG, Xiao-Dong** [CN/US]; 2833 Bryant Street, Palo Alto, CA 94306 (US). **CHEN, Francine** [US/US]; 2660 31st Avenue, San Francisco, CA 94116 (US). **GAZIT, Gadi** [US/US]; 521 Del Medio Avenue, #118, Mountain View, CA 94040 (US). **WEBER, Richard** [US/US]; 2537 Pacheco Street, San Francisco, CA 94116 (US). **BEZABEH, Binyam** [US/US]; 314 Perkins Street, #105, Oakland, CA 94610 (US).

(74) Agent: **HUNT, Dale, C.**; Knobbe, Martens, Olson & Bear, LLP, 2040 Main Street, 14th Floor, Irvine, CA 92614 (US).

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(54) Title: ANTIBODIES DIRECTED TO PDGFD AND USES THEREOF

CTAAAAAATATGTTCTCTACAACACCAAGGCTCATTAAAATATTTTAAATATTAATATACAT
TTCTTCTGTCAGAAATACATAAAACTTTATTATATCAGCGCAGGGCGGCGCGGCGTCGGTCC
CGGGAGCAGAACCCGGCTTTTTCTTGGAGCGACGCTGTCTCTAGTCGCTGATCCCAAATGCA
CCGGCTCATCTTTGTCTACACTCTAATCTGCGCAAACTTTTGCAGCTGTCGGGACACTTCTG
CAACCCCGCAGAGCGCATCCATCAAAGCTTTGCGCAACGCCAACCTCAGGCGAGATGAGAGC
AATCACCTCACAGACTTGTACCGAAGAGATGAGACCATCCAGGTGAAAGGAAACGGCTACGT
GCAGAGTCCTAGATTCCCGAACAGCTACCCCAGGAACCTGCTCCTGACATGGCGGCTTCACT
CTCAGGAGAATACACGGATACAGCTAGTGTTTGACAATCAGTTTGGATTAGAGGAAGCAGAA
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TTAAAATCACATTCAAGTCCGATGACTACTTTGTGGCTAAACCTGGATTCAAGATTTATTAT
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CTCTATTTCAGGGGTATCCTATAACTCTCCATCAGTAACGGATCCCACTCTGATTGCGGATG
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CTGGAGGTCCTGCACATGCAATTCAGGGAAAACCGTGAAAAAGTATCATGAGGTATTACAGT
TTGAGCCTGGCCACATCAAGAGGAGGGGTAGAGCTAAGACCATGGCTCTAGTTGACATCCAG
TTGGATCACCATGAACGATGTGATTGTATCTGCAGCTCAAGACCACCTCGATAAGAGAATGT
GCACATCCTTACATTAAGCCTGAAAGAACCTTTAGTTTAAGGAGGGTGAGATAAGAGACCCT
TTTCCTACCAGCAACCAAACTTACTACTAGCCTGCAATGCAATGAACACAAGTGGTTGCTGA
GTCTCAGCCTTGCTTTGTTAATGCCATGGCAAGTAGAAAGGTATATCATCAACTTCTATACC
TAAGAATATAGGATTGCATTTAATAATAGTGTTTGAGGTTATATATGCACAAACACACACAG
AAATATATTCATGTCTATGTGTATATAGATCAAATGTTTTTTTGGTATATATAACCAGGTA
CACCAGAGCTTACATATGTTTGAGTTAGACTCTTAAAATCCTTTGCCAAAATAAGGGATGGT
CAAATATATGAAACATGTCTTTAGAAAATTTAGGAGATAAATTTATTTTTAAATTTTGAAAC
ACAAAACAATTTTGAATCTTGCTCTCTTAAAGAAAGCATCTTGTATATTAAAAATCAAAAGA
TGAGGCTTTCTTACATATACATCTTAGTTG (SEQ ID NO:50)

(57) Abstract: The present invention is related to antibodies directed to the antigen PDGFD and uses of such antibodies. In particular, in accordance with the present invention, there are provided fully human monoclonal antibodies directed to the antigen PDGFD. Nucelotide sequences encoding, and amino acid sequences comprising, heavy and light chain immunoglobulin molecules, particularly sequences corresponding to contiguous heavy and light chain sequences spanning the framework regions and/or complementarity determining regions (CDR's), specifically from FR1 through FR4 or CDR1 through CDR3, are provided. Hybridomas or other cell lines expressing such immunoglobulin molecules and monoclonal antibodies are also provided.

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ANTIBODIES DIRECTED TO PDGFD AND USES THEREOF

BACKGROUND OF THE INVENTION

1. *Summary of the Invention*

The present invention is related to antibodies directed to the antigen PDGFD and uses of such antibodies. In particular, in accordance with the present invention, there are provided fully human monoclonal antibodies directed to the antigen PDGFD. Nucelotide sequences encoding, and amino acid sequences comprising, heavy and light chain immunoglobulin molecules, particularly sequences corresponding to contiguous heavy and light chain sequences spanning the framework regions and/or complementarity determining regions (CDR's), specifically from FR1 through FR4 or CDR1 through CDR3, are provided. Hybridomas or other cell lines expressing such immunoglobulin molecules and monoclonal antibodies are also provided.

2. *Background of the Technology*

Polypeptide growth factors exerting effects in a variety of tissues have been described. Such growth factors include platelet-derived growth factor (PDGF).

The platelet derived growth factor (PDGF) family currently consists of at least 3 distinct genes, PDGF A, PDGF B, and PDGF C whose gene products selectively signal through two PDGFRs to regulate diverse cellular functions. PDGF A, PDGF B, and PDGF C dimerize in solution to form homodimers, as well as the heterodimer.

Expression of RNA encoding the PDGF A and PDGF B subunits of has been reported in vascular tissues involved in atherosclerosis. PDGF A and PDGF B mRNA have been reported to be present in mesenchymal-appearing intimal cells and endothelial cells, respectively, of atherosclerotic plaques. In addition, PDGF receptor mRNA has also been localized predominantly in plaque intimal cells.

The PDGF B is related to the transforming gene (v-sis) of simian sarcoma virus. The PDGF B has also been reported to be mitogen for cells of mesenchymal origin. The PDGF B has in addition been implicated in autocrine growth stimulation in the pathologic proliferation of endothelial cells characteristically found in glioblastomas. PDGF has also been reported to promote cellular proliferation and inhibits apoptosis.

A novel PDGF, PDGF-D, has recently been cloned and characterized. *See* LaRochelle et al. *Nature Cell Biology* 3:517 (2001), GenBank Accession No. AF335584, International Patent Application No. WO 01/25433, USSN 60/158,083, filed October 7, 1999; USSN 60/159,231, filed October 13, 1999; USSN 60/174,485 filed January 4, 2000; USSN 60/186,707 filed March 3, 2000; USSN 60/188,250, filed March 10, 2000; USSN 60/223,879, filed August 8, 2000; USSN 60/234,082, filed on September 20, 2000; USSN 09/685,330, filed on October 5, 2000; PCT Application US00/27671, filed October 6, 2000; USSN 09/688,312, filed October 13, 2000 and USSN

09/715,332, filed November 16, 2000. Because of its expression profile and sequence homology and/or similarity to the above-discussed genes and gene products, antibodies to the PDGF-D antigen could be useful therapeutically.

BRIEF DESCRIPTION OF THE DRAWING FIGURES

Figure 1 is a representation of the nucleotide sequence of the human PDGFD gene (SEQ ID NO:50).

Figure 2 is a representation of the nucleotide (SEQ ID NO:50) and deduced amino acid (SEQ ID NO:12) sequence of the human PDGF D gene.

Figure 3 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.6 of the invention, with Figure 3A representing the nucleotide sequence encoding the variable region of the heavy chain (SEQ.ID.NO: 55), Figure 3B (SEQ.ID.NO: 13) representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 3A, Figure 3C (SEQ.ID.NO: 56) representing the nucleotide sequence encoding the variable region of the light chain, and Figure 3D (SEQ.ID.NO: 14) representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 3C.

Figure 4 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.11 of the invention, with Figure 4A representing the nucleotide sequence encoding the variable region of the heavy chain (SEQ.ID.NO: 57)Figure 4B (SEQ.ID.NO: 15) representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 4A, Figure 4C (SEQ.ID.NO: 58) representing the nucleotide sequence encoding the variable region of the light chain, and Figure 4D (SEQ.ID.NO: 16) representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 4C.

Figure 5 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.17 of the invention, with Figure 5A (SEQ.ID.NO: 59) representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 5B (SEQ.ID.NO: 17) representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 5A, Figure 5C (SEQ.ID.NO: 60) representing the nucleotide sequence encoding the variable region of the light chain, and Figure 5D (SEQ.ID.NO: 18) representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 5C.

Figure 6 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.18 of the invention, with Figure 6A (SEQ.ID.NO: 61) representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 6B (SEQ.ID.NO: 19)

representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 6A, Figure 6C (SEQ.ID.NO: 62) representing the nucleotide sequence encoding the variable region of the light chain, and Figure 6D (SEQ.ID.NO: 20) representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 6C.

Figure 7 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.19 of the invention, with Figure 7A (SEQ.ID.NO: 63) representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 7B (SEQ.ID.NO: 21) representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 7A, Figure 7C (SEQ.ID.NO: 64) representing the nucleotide sequence encoding the variable region of the light chain, and Figure 7D (SEQ.ID.NO: 22) representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 7C.

Figure 8 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.23 of the invention, with Figure 8A (SEQ.ID.NO: 65) representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 8B (SEQ.ID.NO: 23) representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 8A, Figure 8C (SEQ.ID.NO: 66) representing the nucleotide sequence encoding the variable region of the light chain, and Figure 8D (SEQ.ID.NO: 24) representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 8C.

Figure 9 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.24 of the invention, with Figure 9A (SEQ.ID.NO: 67) representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 9B (SEQ.ID.NO: 25) representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 9A, Figure 9C (SEQ.ID.NO: 68) representing the nucleotide sequence encoding the variable region of the light chain, and Figure 9D (SEQ.ID.NO: 26) representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 9C.

Figure 10 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.25 of the invention, with Figure 10A (SEQ.ID.NO: 69) representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 10B (SEQ.ID.NO: 27) representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 10A, Figure 10C (SEQ.ID.NO: 70) representing the nucleotide sequence encoding the variable region of the light chain, and Figure 10D (SEQ.ID.NO: 28) representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 10C.

Figure 11 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.29 of the invention, with Figure 11A (SEQ.ID.NO: 71) representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 11B (SEQ.ID.NO: 29) representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 11A, Figure 11C (SEQ.ID.NO: 72) representing the nucleotide sequence encoding the variable region of the light chain, and Figure 11D (SEQ.ID.NO: 30) representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 11C.

Figure 12 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.33 of the invention, with Figure 12A (SEQ.ID.NO: 73) representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 12B (SEQ.ID.NO: 31) representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 12A, Figure 12C (SEQ.ID.NO: 74) representing the nucleotide sequence encoding the variable region of the light chain, and Figure 12D (SEQ.ID.NO: 32) representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 12C.

Figure 13 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.38 of the invention, with Figure 13A (SEQ.ID.NO: 75) representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 13B (SEQ.ID.NO: 33) representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 13A, Figure 13C (SEQ.ID.NO: 76) representing the nucleotide sequence encoding the variable region of the light chain, and Figure 13D (SEQ.ID.NO: 34) representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 13C.

Figure 14 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.39 of the invention, with Figure 14A (SEQ.ID.NO: 77) representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 14B (SEQ.ID.NO: 35) representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 14A, Figure 14C (SEQ.ID.NO: 78) representing the nucleotide sequence encoding the variable region of the light chain, and Figure 14D (SEQ.ID.NO: 36) representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 14C.

Figure 15 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.40 of the invention, with Figure 15A (SEQ.ID.NO: 79) representing the

nucleotide sequence encoding the variable region of the heavy chain and Figure 15B (SEQ.ID.NO: 37) representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 15A.

Figure 16 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.45 of the invention, with Figure 16A (SEQ.ID.NO: 80) representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 16B (SEQ.ID.NO: 38) representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 16A, Figure 16C (SEQ.ID.NO: 81) representing the nucleotide sequence encoding the variable region of the light chain, and Figure 16D (SEQ.ID.NO: 39) representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 16C.

Figure 17 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.46 of the invention, with Figure 17A (SEQ.ID.NO: 82) representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 17B (SEQ.ID.NO: 40) representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 17A, Figure 17C (SEQ.ID.NO: 83) representing the nucleotide sequence encoding the variable region of the light chain, and Figure 17D (SEQ.ID.NO: 41) representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 17C.

Figure 18 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.48 of the invention, with Figure 18A (SEQ.ID.NO: 84) representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 18B (SEQ.ID.NO: 42) representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 18A, Figure 18C (SEQ.ID.NO: 85) representing the nucleotide sequence encoding the variable region of the light chain, and Figure 18D (SEQ.ID.NO: 43) representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 18C.

Figure 19 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.49 of the invention, with Figure 19A (SEQ.ID.NO: 86) representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 19B (SEQ.ID.NO: 44) representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 19A, Figure 19C (SEQ.ID.NO: 87) representing the nucleotide sequence encoding the variable region of the light chain, and Figure 19D (SEQ.ID.NO: 45) representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 19C.

Figure 20 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma

cell line designated Cur 2-1.51 of the invention, with Figure 20A (SEQ.ID.NO: 88) representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 20B (SEQ.ID.NO: 46) representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 20A, Figure 20C (SEQ.ID.NO: 89) representing the nucleotide sequence encoding the variable region of the light chain, and Figure 20D (SEQ.ID.NO: 47) representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 20C.

Figure 21 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-6.4 of the invention, with Figure 21A (SEQ.ID.NO: 90) representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 21B (SEQ.ID.NO: 48) representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 21A, Figure 21C (SEQ.ID.NO: 91) representing the nucleotide sequence encoding the variable region of the light chain, and Figure 21D (SEQ.ID.NO: 49) representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 21C.

Figure 22 is a table showing VDJ gene utilization of antibodies of the invention and indicating nucleotide/amino acid changes between the antibodies and the V, D, or J genes from which they are derived in the antibodies FR1, CDR1, FR2, CDR2, FR3, CDR3, and FR4 regions.

Figure 23 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.6 of the invention and the V gene from which it is derived. Figure 23A represents the alignment of the heavy chain amino acid sequence CUR2.1.6.1 HC (SEQ. ID. NO: 270) and VH2-21 (SEQ. ID. NO: 271), the consensus being shown below (SEQ. ID. NO: 272). Figure 23B represents the alignment of the light chain amino acid sequence of .CUR2.1.6.1 LC (SEQ. ID. NO: 273) and A30 (SEQ. ID. NO: 274), with the consensus sequence being shown below (SEQ. ID. NO: 275).

Figure 24 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.11 of the invention and the V gene from which it is derived. Figure 24A represents the alignment of the heavy chain amino acid sequence CUR2.1.11.1 HC (SEQ. ID. NO: 276) and VH3-53 (SEQ. ID. NO: 277), the consensus being shown below (SEQ. ID. NO: 278). Figure 24B represents the alignment of the light chain amino acid sequence of CUR2.1.11.1 LC (SEQ. ID. NO: 279) and A19 (SEQ. ID. NO: 280), with the consensus sequence shown below (SEQ. ID. NO: 281).

Figure 25 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated CR 2-1.17.1 of the invention and the V gene from which it is derived. Figure 25A represents the alignment of the heavy chain amino acid sequence CR 2-1.17.1 HC (SEQ. ID. NO: 282) and VH3-53 (SEQ. ID. NO:283), the consensus being shown below (SEQ. ID. NO: 284). Figure 25B represents

the alignment of the light chain amino acid sequence of CR 2-1.17.1 LC (SEQ. ID. NO: 285) and A30 (SEQ. ID. NO: 286), with the consensus sequence being shown below (SEQ. ID. NO: 287).

Figure 26 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.18 of the invention and the V gene from which it is derived.Figure 26A represents the alignment of the heavy chain amino acid sequence CR2-1.18 HC (SEQ. ID. NO: 288) and VH1-8 (SEQ. ID. NO: 289), the consensus being shown below (SEQ. ID. NO: 290). Figure 26B represents the alignment of the light chain amino acid sequence of CR2-1.18 LC (SEQ. ID. NO: 291) and A30 (SEQ. ID. NO: 292), with the consensus sequence being shown below (SEQ. ID. NO: 293).

Figure 27 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.19 of the invention and the V gene from which it is derived Figure 27A represents the alignment of the heavy chain amino acid sequence CUR2.1.19.1 HC (SEQ. ID. NO: 294) and VH1-8 (SEQ. ID. NO: 295), the consensus being shown below (SEQ. ID. NO: 296). Figure 27B represents the alignment of the light chain amino acid sequence of CUR2.1.19.1 LC (SEQ. ID. NO: 297) and A30 (SEQ. ID. NO: 298), with the consensus sequence being shown below (SEQ. ID. NO: 299).

Figure 28 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.23 of the invention and the V gene from which it is derived. Figure 28A represents the alignment of the heavy chain amino acid sequence CUR2.1.23.1 HC (SEQ. ID. NO: 300) and VH5-51 (SEQ. ID. NO: 301), the consensus being shown below (SEQ. ID. NO: 302). Figure 28B represents the alignment of the light chain amino acid sequence of CUR2.1.23.1 LC (SEQ. ID. NO: 303) and A30 (SEQ. ID. NO: 304), with the consensus sequence being shown below (SEQ. ID. NO: 305).

Figure 29 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.24 of the invention and the V gene from which it is derived. Figure 29A represents the alignment of the heavy chain amino acid sequence CUR2.1.24.1 HC (SEQ. ID. NO: 306) and VH3-33 (SEQ. ID. NO: 307), the consensus being shown below (SEQ. ID. NO: 308). Figure 29B represents the alignment of the light chain amino acid sequence of CUR2.1.24.1 LC (SEQ. ID. NO: 309) and A30 (SEQ. ID. NO: 310), with the consensus sequence being shown below (SEQ. ID. NO: 311).

Figure 30 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.25 of the invention and the V gene from which it is derived. Figure 30A represents the alignment of the heavy chain amino acid sequence VH5-51 (SEQ. ID. NO: 312) and CUR2.1.25.1 HC (SEQ. ID. NO: 313), the consensus being shown below (SEQ. ID. NO: 314). Figure 30B represents

the alignment of the light chain amino acid sequence of A30 (SEQ. ID. NO: 315) and CUR2.1.25.1 LC (SEQ. ID. NO: 316), with the consensus sequence shown below (SEQ. ID. NO: 317).

Figure 31 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.29 of the invention and the V gene from which it is derived. Figure 31A represents the alignment of the heavy chain amino acid sequence VH5-51 (SEQ. ID. NO: 318) and CUR2.1.29 HC (SEQ. ID. NO: 319), the consensus being shown below (SEQ. ID. NO: 320). Figure 31B represents the alignment of the light chain amino acid sequence of A19 (SEQ. ID. NO: 321) and CUR2.1.29 LC (SEQ. ID. NO: 322), with the consensus sequence being shown below (SEQ. ID. NO: 323).

Figure 32 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.33 of the invention and the V gene from which it is derived. Figure 32A represents the alignment of the heavy chain amino acid sequence VH1-18 (SEQ. ID. NO: 324) and CR2.1.33 HC (SEQ. ID. NO: 325), the consensus being shown below (SEQ. ID. NO: 326). Figure 32B represents the alignment of the light chain amino acid sequence of A20 (SEQ. ID. NO: 327) and CR2.1.33 LC (SEQ. ID. NO: 328), with the consensus sequence being shown below (SEQ. ID. NO: 329).

Figure 33 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.38 of the invention and the V gene from which it is derived. Figure 33A represents the alignment of the heavy chain amino acid sequence VH3-33 (SEQ. ID. NO: 330) and CR2.1.38.1 HC (SEQ. ID. NO: 331), the consensus being shown below (SEQ. ID. NO: 332). Figure 33B represents the alignment of the light chain amino acid sequence of A20 (SEQ. ID. NO: 334) and CUR2.1.38.1 LC (SEQ. ID. NO: 335), with the consensus sequence being shown below (SEQ. ID. NO: 336).

Figure 34 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.39 of the invention and the V gene from which it is derived. Figure 34A represents the alignment of the heavy chain amino acid sequence VH5-51 (SEQ. ID. NO: 336) and CR2.1.39.1 HC (SEQ. ID. NO: 337), the consensus being shown below (SEQ. ID. NO: 338). Figure 34B represents the alignment of the light chain amino acid sequence of A30 (SEQ. ID. NO: 339) and CR2.1.39.1 LC (SEQ. ID. NO: 340), with the consensus sequence being shown below (SEQ. ID. NO: 341).

Figure 35 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.45 of the invention and the V gene from which it is derived. Figure 35A represents the alignment of the heavy chain amino acid sequence VH1-8 (SEQ. ID. NO: 342) and CR2.1.45.1 HC (SEQ. ID. NO: 343), the consensus being shown below (SEQ. ID. NO: 344). Figure 35B represents

the alignment of the light chain amino acid sequence of A20 (SEQ. ID. NO: 345) and CUR2.1.45.1 LC (SEQ. ID. NO: 346), with the consensus sequence being shown below (SEQ. ID. NO: 347).

Figure 36 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.46 of the invention and the V gene from which it is derived. Figure 36A represents the alignment of the heavy chain amino acid sequence VH1-8 (SEQ. ID. NO: 348) and CR2.1.46.1 HC (SEQ. ID. NO: 349), the consensus being shown below (SEQ. ID. NO: 350). Figure 36B represents the alignment of the light chain amino acid sequence of A30 (SEQ. ID. NO: 351) and CR2.1.46.1 LC (SEQ. ID. NO: 352), with the consensus sequence being shown below (SEQ. ID. NO: 353).

Figure 37 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.48 of the invention and the V gene from which it is derived. Figure 37A represents the alignment of the heavy chain amino acid sequence CR2.1.48.1 HC (SEQ. ID. NO: 354) and VH1-18 (SEQ. ID. NO: 355), the consensus being shown below (SEQ. ID. NO:.356). Figure 37B represents the alignment of the light chain amino acid sequence of CR2.1.48.1 LC (SEQ. ID. NO: 357) and L5 (SEQ. ID. NO: 358), with the consensus sequence being shown below (SEQ. ID. NO: 359).

Figure 38 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.49 of the invention and the V gene from which it is derived. Figure 38A represents the alignment of the heavy chain amino acid sequence CR2.1.49.1 HC (SEQ. ID. NO: 360) and VH1-8 (SEQ. ID. NO: 361), the consensus being shown below (SEQ. ID. NO: 362). Figure 38B represents the alignment of the light chain amino acid sequence of CUR2.1.49.1 LC (SEQ. ID. NO: 363) and A19 (SEQ. ID. NO: 364), with the consensus sequence being shown below (SEQ. ID. NO: 365).

Figure 39 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.51 of the invention and the V gene from which it is derived. Figure 39A represents the alignment of the heavy chain amino acid sequence CR2.1.51.1 HC (SEQ. ID. NO: 366) and VH5-51 (SEQ. ID. NO: 367), the consensus being shown below (SEQ. ID. NO: 368). Figure 39B represents the alignment of the light chain amino acid sequence of CR2.1.51.1 LC (SEQ. ID. NO: 369) and A27 (SEQ. ID. NO: 370), with the consensus sequence being shown below (SEQ. ID. NO: 371).

Figure 40 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-6.4 of the invention and the V gene from which it is derived. Figure 40A represents the alignment of the heavy chain amino acid sequence CUR2.6.4.1 HC (SEQ. ID. NO: 372) and VH1-8 (SEQ. ID. NO: 373), the consensus being shown below (SEQ. ID. NO: 374). Figure 40B represents

the alignment of the light chain amino acid sequence of CUR2.6.4.1 LC (SEQ. ID. NO: 375) and A27 (SEQ. ID. NO: 376), with the consensus sequence being shown below (SEQ. ID. NO: 377).

Figure 41 is a table showing VDJ gene utilization of the 1.19.1 and 6.4.1 antibodies of the invention and indicating nucleotide changes between the antibodies and the VH, DH, and JH and VK and JK genes from which they are derived.

Figure 42 is a table showing VDJ gene utilization of the 1.6.1, 1.11.1, and 1.23.1 antibodies of the invention and indicating nucleotide changes between the antibodies and the VH, DH, and JH and VK and JK genes from which they are derived.

Figure 43 is a table showing VDJ gene utilization of the 1.19.1, 6.4.1, 1.6.1, 1.11.1, 1.23.1, 1.17.1, 1.18, 1.24.1, 1.25.1, 1.29, 1.33, 1.38.1, 1.39.1, 1.40.1, 1.45, 1.46.1, 1.46.2, 1.48.1, 1.49.1, and 1.51.1 antibodies of the invention and indicating nucleotide changes between the antibodies and the VH, DH, and JH and VK and JK genes from which they are derived.

Figure 44 is a bar graphic representation comparing the levels of BrdU incorporation in NIH 3T3 cells upon exposure to various human anti-PDGFD monoclonal antibodies of the invention.

Figure 45 is a bar graphic representation comparing the levels of BrdU incorporation in NIH 3T3 cells upon exposure to various human anti-PDGFD monoclonal antibodies of the invention at varying doses as compared to a control run utilizing PDGFBB at varying concentrations.

Figure 46 is a bar graphic representation comparing the levels of BrdU incorporation in NIH 3T3 cells upon exposure to various human anti-PDGFD monoclonal antibodies of the invention at varying doses as compared to a control run utilizing PDGFBB at varying concentrations.

Figure 47 is a bar graphic representation comparing the levels of BrdU incorporation in NIH 3T3 cells upon exposure to various human anti-PDGFD monoclonal antibodies of the invention at varying doses as compared to a control run utilizing PDGFBB at varying concentrations.

Figure 48 is a representation of a ClustalW sequence alignment between the heavy chain amino acid sequences of antibodies of the invention indicating locations of the CDRs of the antibodies. Heavy chain sequences shown are: 1.19H (SEQ. ID. NO: 199); 6.4H (SEQ. ID. NO: 200); 1.18H (SEQ. ID. NO: 201); 1.40H (SEQ. ID. NO: 202); 145H (SEQ. ID. NO: 203); 1.46H (SEQ. ID. NO: 204); 1.49H (SEQ. ID. NO: 205); 1.33H (SEQ. ID. NO: 206); 1.48H (SEQ. ID. NO: 207); 1.6H (SEQ. ID. NO: 208); 1.17H (SEQ. ID. NO: 209); 1.24H (SEQ. ID. NO: 210); 1.38H (SEQ. ID. NO: 211); 1.11H (SEQ. ID. NO: 212); 1.23H (SEQ. ID. NO: 213); 1.25H (SEQ. ID. NO: 214); 1.29H (SEQ. ID. NO: 215); 1.39H (SEQ. ID. NO: 216); and 1.51H (SEQ. ID. NO: 217).

Figure 49 is a representation of a ClustalW sequence alignment between the light chain amino acid sequences of antibodies of the invention indicating locations of the CDRs of the antibodies. Light chain sequences shown are: 1.48L (SEQ. ID. NO: 218); 1.49L (SEQ. ID. NO: 219); 1.11L (SEQ. ID. NO: 220); 1.29L (SEQ. ID. NO: 221); 1.45L (SEQ. ID. NO: 222); 1.33L (SEQ. ID. NO: 223); 1.38L (SEQ. ID. NO: 224); 6.4L (SEQ. ID. NO: 225); 1.51L (SEQ. ID. NO: 226); 1.19L (SEQ.

ID. NO: 227); 1.18L (SEQ. ID. NO: 228); 1.16L (SEQ. ID. NO: 229); 1.23L (SEQ. ID. NO: 230); 1.25L (SEQ. ID. NO: 231); 1.39L (SEQ. ID. NO: 232); 1.17L (SEQ. ID. NO: 233); 1.24L (SEQ. ID. NO: 234); and 1.46L (SEQ. ID. NO: 235).

Figure 50 is a representation of a ClustalW sequence alignment between the heavy chain amino acid sequences of antibodies of the invention that possess heavy chains derived from the VH 1-8 gene with CDRs indicated. Heavy chain sequences shown are: 1.19H (SEQ. ID. NO: 236); 6.4H (SEQ. ID. NO: 237); 1.18H (SEQ. ID. NO: 238); 1.40H (SEQ. ID. NO: 239); 1.45H (SEQ. ID. NO: 240); 1.46H (SEQ. ID. NO: 241); and 1.49H (SEQ. ID. NO: 242).

Figure 51 is a representation of a ClustalW sequence alignment between the heavy chain amino acid sequences of antibodies of the invention that possess heavy chains derived from the VH 1-18 gene with CDRs indicated. Heavy chain sequences shown are: 1.33H (SEQ. ID. NO: 243) and 1.48H (SEQ. ID. NO: 244).

Figure 52 is a representation of a ClustalW sequence alignment between the heavy chain amino acid sequences of antibodies of the invention that possess heavy chains derived from the VH 3-33 gene with CDRs indicated. Heavy chain sequences shown are: 1.17H (SEQ. ID. NO: 245); 1.24H (SEQ. ID. NO: 246); and 1.38H (SEQ. ID. NO: 247).

Figure 53 is a representation of a ClustalW sequence alignment between the heavy chain amino acid sequences of antibodies of the invention that possess heavy chains derived from the VH 5-51 gene with CDRs indicated. Heavy chain sequences shown are: 1.23H (SEQ. ID. NO: 248); 1.25H (SEQ. ID. NO: 249); 1.29H (SEQ. ID. NO: 250); 1.39H (SEQ. ID. NO: 251); and 1.51H (SEQ. ID. NO: 252).

Figure 54 is a representation of a ClustalW sequence alignment between the light chain amino acid sequences of antibodies of the invention that possess light chains derived from the VK A19 gene with CDRs indicated. Light chain sequences shown are: 1.49L (SEQ. ID. NO: 253); 1.11L (SEQ. ID. NO: 254); and 1.29L (SEQ. ID. NO: 255).

Figure 55 is a representation of a ClustalW sequence alignment between the light chain amino acid sequences of antibodies of the invention that possess light chains derived from the VK A20 gene with CDRs indicated. Light chain sequences shown are: 1.45L (SEQ. ID. NO: 256); 1.33L (SEQ. ID. NO: 257); and 1.38L (SEQ. ID. NO: 258).

Figure 56 is a representation of a ClustalW sequence alignment between the light chain amino acid sequences of antibodies of the invention that possess light chains derived from the VK A27 gene with CDRs indicated. Light chain sequences shown are: 6.4L (SEQ. ID. NO: 259) and 1.51L (SEQ. ID. NO: 260).

Figure 57 is a representation of a ClustalW sequence alignment between the light chain amino acid sequences of antibodies of the invention that possess light chains derived from the VK A30 gene with CDRs indicated. Light chain sequences shown are: 1.19L (SEQ. ID. NO: 261); 1.18L (SEQ. ID.

NO: 262); 1.16L (SEQ. ID. NO: 263); 1.23L (SEQ. ID. NO: 264); 1.25L (SEQ. ID. NO: 265); 1.39L (SEQ. ID. NO: 266); 1.17L (SEQ. ID. NO: 267); 1.24L (SEQ. ID. NO: 268); and 1.46L (SEQ. ID. NO: 269).

SUMMARY OF THE INVENTION

In accordance with a first aspect of the present invention, there is provided a human monoclonal antibody that binds to PDGFD and has a heavy chain amino acid sequence selected from the group consisting of SEQ ID NOS: 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 38, 40, 42, 44, 46, and 48. In one embodiment, the antibody further comprises a light chain amino acid sequence selected from the group consisting of SEQ ID NOS: 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 39, 41, 43, 45, 47, and 49.

In accordance with a second aspect of the present invention there is provided a human antibody that binds to PDGFD that comprises a heavy chain amino acid sequence corresponding substantially to the amino acid sequence encoded by the VH 1-8 gene and any of the amino acid differences shown in Figure 50 and comprising a CDR3 sequence selected from the group consisting of the CDR3 sequences shown in Figure 50.

In accordance with a third aspect of the present invention there is provided a human antibody that binds to PDGFD that comprises a heavy chain amino acid sequence corresponding substantially to the amino acid sequence encoded by the VH 1-18 gene and any of the amino acid differences shown in Figure 51 and comprising a CDR3 sequence selected from the group consisting of the CDR3 sequences shown in Figure 51.

In accordance with a fourth aspect of the present invention there is provided a human antibody that binds to PDGFD that comprises a heavy chain amino acid sequence corresponding substantially to the amino acid sequence encoded by the VH 3-33 gene and any of the amino acid differences shown in Figure 52 and comprising a CDR3 sequence selected from the group consisting of the CDR3 sequences shown in Figure 52.

In accordance with a fifth aspect of the present invention there is provided a human antibody that binds to PDGFD that comprises a heavy chain amino acid sequence corresponding substantially to the amino acid sequence encoded by the VH 5-51 gene and any of the amino acid differences shown in Figure 53 and comprising a CDR3 sequence selected from the group consisting of the CDR3 sequences shown in Figure 53.

In accordance with a sixth aspect of the present invention there is provided a human antibody that binds to PDGFD that comprises a light chain amino acid sequence corresponding substantially to the amino acid sequence encoded by the VK A19 gene and any of the amino acid differences shown in Figure 54 and comprising a CDR3 sequence selected from the group consisting of the CDR3 sequences shown in Figure 54.

In accordance with a seventh aspect of the present invention there is provided a human antibody that binds to PDGFD that comprises a light chain amino acid sequence corresponding substantially to the amino acid sequence encoded by the VK A20 gene and any of the amino acid differences shown in Figure 55 and comprising a CDR3 sequence selected from the group consisting of the CDR3 sequences shown in Figure 55.

In accordance with an eighth aspect of the present invention there is provided a human antibody that binds to PDGFD that comprises a light chain amino acid sequence corresponding substantially to the amino acid sequence encoded by the VK A27 gene and any of the amino acid differences shown in Figure 56 and comprising a CDR3 sequence selected from the group consisting of the CDR3 sequences shown in Figure 56.

In accordance with a ninth aspect of the present invention there is provided a human antibody that binds to PDGFD that comprises a light chain amino acid sequence corresponding substantially to the amino acid sequence encoded by the VK A30 gene and any of the amino acid differences shown in Figure 57 and comprising a CDR3 sequence selected from the group consisting of the CDR3 sequences shown in Figure 57.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

A novel PDGF, PDGF-D, has recently been cloned and characterized. *See* LaRochelle et al. *Nature Cell Biology* 3:517 (2001), GenBank Accession No. AF335584, International Patent Application No. WO 01/25433, USSN 60/158,083, filed October 7, 1999; USSN 60/159,231, filed October 13, 1999; USSN 60/174,485 filed January 4, 2000; USSN 60/186,707 filed March 3, 2000; USSN 60/188,250, filed March 10, 2000; USSN 60/223,879, filed August 8, 2000; USSN 60/234,082, filed on September 20, 2000; USSN 09/685,330, filed on October 5, 2000; PCT Application US00/27671, filed October 6, 2000; USSN 09/688,312, filed October 13, 2000 and USSN 09/715,332, filed November 16, 2000. Because of its expression profile and sequence homology and/or similarity to the above-discussed genes and gene products, antibodies to the PDGF-D antigen could be useful therapeutically. Because of its expression profile and sequence homology and/or similarity to the above-discussed genes and gene products, antibodies to the PDGF-D antigen could be useful therapeutically.

The nucleotide and translated amino acid sequence, respectively, of PDGF-D is set forth in Figures 1 and 2.

The similarities of the disclosed PDGFD polypeptides to previously described BMP-1 VEGF-E and PDGF polypeptides indicate a similarity of functions by the PDGFD nucleic acids and polypeptides of the invention. These utilities are described in more detail below.

PDGFD nucleic acids and polypeptides may be use to induce formation of cartilage, as BMP-1 is also capable of inducing formation of cartilage *in vivo* (Wozney *et al.*, *Science* 242: 1528-1534 (1988)).

An additional use for the PDGFD nucleic acids and polypeptides is in the modulation of collagen formation. Recombinantly expressed BMP1 and purified procollagen C proteinase (PCP), a secreted metalloprotease requiring calcium and needed for cartilage and bone formation, are, in fact, identical. See, Kessler *et al.*, *Science* 271:360-62 (1996). BMP-1 cleaves the C-terminal propeptides of procollagen I, II, and III and its activity is increased by the procollagen C-endopeptidase enhancer protein. PDGFD nucleic acids and polypeptides may play similar roles in collagen modulation pathways.

PDGFD nucleic acids and polypeptides can also be used to stage various cancers. For example, bone metastases can almost universally be correlated to the morbidity and mortality of certain prostate cancers. For example, bone morphogenetic proteins are implicated as having important roles in various cancers. Overexpression of bone morphogenetic protein-4 ("BMP-4") and BMP-2 mRNA has been reported in gastric cancer cell lines of poorly differentiated type. See, Katoh *et al.*, *J. Gastroenterol* 31(1):137-9 (1996). This observation may have implications regarding the poor prognosis of patients with diffuse osteoplastic bone metastasis of gastric cancer. Additionally, osteosarcomas producing bone morphogenetic protein ("BMP") differed in clinical features from those not producing BMP. See, Yoshikawa *et al Cancer* 56: 1682-7 (1985) They were characterized radiologically by perpendicular spicules, histologically by osteoblastic type cells, and clinically by an increased serum alkaline phosphatase level, relative resistance to preoperative chemotherapy with Adriamycin (doxorubicin) plus high-dose methotrexate, and a tendency to metastasize to other bones and the lungs.

The relatedness of PDGFD polypeptides to VEGF- reveals uses for PDGFD nucleic acids and polypeptides in modulating angiogenesis. Angiogenesis is a process which contributes to the development of new blood vessels. During angiogenesis, new capillaries sprout from existing vessels. See, Risau *FASEB J.* 9(10): 926-33 (1995); Risau *et al.*, *Ann.Rev. Cell Dev Biol.* 11: 73-91 (1995). In adult mammals, new blood vessels are produced through angiogenesis. Pathological states in which angiogenesis contributes to the appearance and maintenance of the pathology include tumor development and growth. vascular endothelial growth factor F has been reported to be involved in angiogenesis.

Vascular endothelial growth factor ("VEGF") is a multifunctional cytokine expressed and secreted at high levels by many tumor cells in both nonhumans and humans. See review in Ferrara, *Curr Top Microbiol Immunol* 237: 1-30 (1999). VEGF exerts its effects on the vascular endothelium through at least two receptors that are expressed on the cell surface. The first is kinase insert domain-containing receptor ("KDR")/fetal liver kinase 1 ("Flk-1"), and the second is FLT-1 (Warren *et al.*, *J Clin Invest* 95: 1789-97 (1995)). These two receptors have different affinities for VEGF and appear to have different cellular responses. See, Athanassiades *et al.*, *Placenta* 19(7): 465-73 (1998); Li *et al.* *Cell Res* 9: 11-25 (1999). FLT-1 null mice die in the embryonic stage, at about day 8.5, whereas KDR

null mice survive through birth and retain endothelial and hematopoietic cell development. Activation of KDR leads to mitogenesis and to up-regulation of e-nitric oxide synthase (eNOS) and inducible NOS, enzymes in the nitric oxide pathway that contribute to regulation of vasodilation and that play a role in vascular tumor development.

It has been also been reported that VEGF acts as a survival factor for newly formed blood vessels. In the developing retina, for example, vascular regression in response to hyperoxia has been correlated with inhibition of VEGF release by glial cells. See, Alon *et al*, *Nat Med* 1: 1024-8(1995). Furthermore, administration of anti-VEGF monoclonal antibodies results in regression of already established tumor-associated vasculature in xenograft models. See, Yuan, *et al.*, *Proc Natl Acad Sci U S A* 93: 14765-70(1996). Therefore, antibodies to PDGFD polypeptides may also be used to induce or promote regression of newly formed blood vessels.

Tumor cells additionally respond to hypoxia by secreting VEGF. This response promotes neovascularization and consequently permits tumor growth. Furthermore, it has been found that several tumor cells, including hematopoietic cells (Bellamy *et al.*, *Cancer Res* 59(3): 728-33 (1999)), breast cancer cells (Speirs *et al.*, *Br J Cancer* 80(5-6): 898-903(1999)), and Kaposi's sarcoma (Masood *et al.*, *Proc Natl Acad Sci U S A* 94(3): 979-84 (1997)), express the KDR receptor. Such results suggest that in these tumors VEGF is acting not only in a paracrine fashion to stimulate angiogenesis, but also via an autocrine mechanism as well to stimulate proliferation and/or survival of endothelial cells, and/or promoting survival of tumor cells. Accordingly, modulation of angiogenesis by PDGFD antibodies, or other antagonists of PDGFD nucleic acid or polypeptide function, can be used in anoxia-associated conditions to inhibit endothelial cell proliferation, and/or tumor cells such as hematopoietic cells, breast cancer cells, and Kaposi's sarcoma cells.

The similarity between PDGFD polypeptides and VEGF polypeptides suggests that PDGFD nucleic acids and their encoded polypeptides can be used to modulate cell survival. It has been reported that VEGF signaling is important for cell survival. Binding of VEGF to its receptor, VEGF receptor-2 (VEGFR-2/Flk1/KDR), is reported to induce the formation of a complex of VE-cadherin, ß-catenin, phosphoinositide-3-OH kinase (PI3-K), and KDR. PI3-K in this complex activates the serine/threonine protein kinase Akt (protein kinase B) by phosphorylation. See, Carmeliet *et al.*, 1999 *Cell* 98(2): 147-57. Activated Akt is then thought to be necessary and sufficient to mediate the VEGF-dependent survival signal. See, Gerber *et al.* 1998 *J. Biol. Chem.* 273(46): 30336-43. These findings indicate that there is a relationship between VEGF signaling and cell survival.

The similarity between PDGFD polypeptides and PDGF polypeptides suggests that PDGFD nucleic acids and their encoded polypeptides can be used in various therapeutic and diagnostic applications. For example, PDGFD nucleic acids and their encoded polypeptides can be used to treat cancer, cardiovascular and fibrotic diseases and diabetic ulcers. In addition, PDGFD nucleic acids and their encoded polypeptides will be therapeutically useful for the prevention of aneurysms and the

acceleration of wound closure through gene therapy. Furthermore, PDGFD nucleic acids and their encoded polypeptides can be utilized to stimulate cellular growth.

PDGFD nucleic acids according to th invention can be used to identify various cell types, including cancerous cells. For example, PDGFD is strongly expressed specifically in CNS cancer, lung cancer and ovarian cancer. It is also shown in the PDGFD produces a gene product which either persists intact in conditioned medium arising from transfecting HEK 293 cells, or is processed to provide fragments of the gene product. The activities ascribed to either one or both of these substances include the ability to stimulate net DNA synthesis as monitored by incorporation of BrdU into DNA, proliferation of cell number, the ability to transform cells in culture, and the ability to induce tumor formation *in vivo*. These various activities occur in a variety of cell types. Additional activities include inducing the phosphorylation of tyrosine residues of receptor protein molecules.

A PDGFD nucleic acid or gene product, is useful as a therapeutic agent in promoting wound healing, neovascularization and tissue growth, and similar tissue regeneration needs. More specifically, a PDGFD nucleic acid or polypeptide may be useful in treatment of anemia and leukopenia, intestinal tract sensitivity and baldness. Treatment of such conditions may be indicated in, *e.g.*, patients having undergone radiation or chemotherapy. It is intended in such cases that administration of a PDGFD nucleic acid or polypeptideor a nucleic acid sequence encoding these polypeptides will be controlled in dose such that any hyperproliferative side effects are minimized.

Alternatively, in cases of tumors, such as CNS cancer and ovarian cancer, in which PDGFD nucleic acids is expressed at high levels it is desired to inhibit or eliminate the effects of production of a PDGFD nucleic acid or gene product. For example, this may be accomplished by administration of an antibody directed against PDGFD identified herein. An alternative example involves identifying the putative protease implicated in the formation of p35 from p85 (*see* WO 01/25433 4/12/2001). Administration of a substance that specifically inhibits the activity of this protease, but not the activity of other proteases, will be effective to prevent formation of the active p35 form of a PDGFD polypeptide.

Based on the roles of molecules related to PDGFD polypeptides and nucleic acids, (*e.g.*, BMP-1 and VEGF-like polypeptides such as fallotein) in malignant disease progression and the gene expression profile described herein, it is foreseen that, for a subset of human gliomas and ovarian epithelial carcinomas, targeting of a PDGFD polypeptide using an antibody has an inhibitory effect on tumor growth, matrix invasion, chemo-resistance, radio-resistance, and metastatic dissemination. In various embodiments, the PDGFD polypeptide is linked to a monoclonal antibody, a humanized antibody or a fully human antibody.

Furthermore, based on chromosomal location analysis (*see* WO 01/25433 4/12/2001) the PDGFD nucleic acids localize to chromosome 11q23-24. This chromosomal locus to D maps is a region of genomic instability (Kurahashi *et al.*, Hum. Mol. Genet. 9, 1665-1670 (2000)) altered in

various neoplasias (Ferti-Passantonopoulou, *et al.* Cancer Genet. Cytogenet. 51, 183-188 (1991); Tarkkanen *et al.*, Genes Chromosomes Cancer 25, 323-331 (1999)) and Jacobsen's syndrome (Pivnick *et al.*, J. Med. Genet. 33, 772-778 (1996)) that might be explained in part through abnormal growth factor expression. Jacobsen's syndrome is marked by craniofacial abnormalities, heart defects, glandular abnormalities and lack of brain development (Pivnick *et al.* (1996)). Accordingly, the PDGFD nucleic acids and polypeptides according to the invention may be used in various diagnostic and therapeutic applications of these disease states.

Additionally, rearrangements resulting in amplification or deletions about the 11q23-24 locus have been reported in breast cancer (Ferti-Passantonopoulou, *et al.* Cancer Genet. Cytogenet. 51, 183-188 (1991); Shen *et al., J. Surg. Oncol.* 74, 100-107 (2000)), primary sarcomas, their pulmonary metastasis (Tarkkanen *et al.* (1999)), and myeloid leukemias (Michaux *et al., Genes Chromosomes Cancer* 29, 40-47 (2000); Crossen, *et al. Cancer Genet. Cytogenet.* 112, 144-148 (1999)). Thus, PDGFD nucleic acids polypeptides and antibodies according to the invention may also have diagnostic and therapeutic applications in the detection and treatment these cancers.

A PDGFD polypeptide can potentially block or limit the extent of tumor neovascularization. In addition to classical modes of administration of potential antibody therapeutics newly developed modalities of administration may be useful. For example, local administration of ^{131}I-labeled monoclonal antibody for treatment of primary brain tumors after surgical resection has been reported. Additionally, direct stereotactic intracerebral injection of monoclonal antibodies and their fragments is also being studied clinically and pre-clinically. Intracarotid hyperosmolar perfusion is an experimental strategy to target primary brain malignancy with drug conjugated human monoclonal antibodies.

Additionally, the nucleic acids of the invention, and fragments and variants thereof, may be used, by way of nonlimiting example, (a) to direct the biosynthesis of the corresponding encoded proteins, polypeptides, fragments and variants as recombinant or heterologous gene products, (b) as probes for detection and quantification of the nucleic acids disclosed herein, (c) as sequence templates for preparing antisense molecules, and the like. Such uses are described more fully in the following disclosure.

Furthermore, the proteins and polypeptides of the invention, and fragments and variants thereof, may be used, in ways that include (a) serving as an immunogen to stimulate the production of an anti-PDGFD antibody, (b) a capture antigen in an immunogenic assay for such an antibody, (c) as a target for screening for substances that bind to a PDGFD polypeptide of the invention, and (d) a target for a PDGFD-specific antibody such that treatment with the antibody inhibits cell growth. These utilities and other utilities for PDGFD nucleic acids, polypeptides, antibodies, agonists, antagonists, and other related compounds uses are disclosed more fully below. In view of its strong effects in modulating cell growth, an increase of PDGFD polypeptide expression or activity can be used to

promote cell survival. Conversely, a decrease in PDGFD polypeptide expression can be used to induce cell death.

PDGFD Agonists And Antagonists

The present invention also pertains to variants of a PDGFD protein that function as either PDGFD agonists (mimetics) or as PDGFD antagonists. Variants of a PDGFD protein can be generated by mutagenesis, *e.g.*, discrete point mutation or truncation of the PDGFD protein. An agonist of the PDGFD protein can retain substantially the same, or a subset of, the biological activities of the naturally occurring form of the PDGFD protein. An antagonist of the PDGFD protein can inhibit one or more of the activities of the naturally occurring form of the PDGFD protein by, for example, competitively binding to a downstream or upstream member of a cellular signaling cascade which includes the PDGFD protein. Thus, specific biological effects can be elicited by treatment with a variant of limited function. In one embodiment, treatment of a subject with a variant having a subset of the biological activities of the naturally occurring form of the protein has fewer side effects in a subject relative to treatment with the naturally occurring form of the PDGFD protein.

Variants of the PDGFD protein that function as either PDGFD agonists (mimetics) or as PDGFD antagonists can be identified by screening combinatorial libraries of mutants, *e.g.*, truncation mutants, of the PDGFD protein for PDGFD protein agonist or antagonist activity. In one embodiment, a variegated library of PDGFD variants is generated by combinatorial mutagenesis at the nucleic acid level and is encoded by a variegated gene library. A variegated library of PDGFD variants can be produced by, for example, enzymatically ligating a mixture of synthetic oligonucleotides into gene sequences such that a degenerate set of potential PDGFD sequences is expressible as individual polypeptides, or alternatively, as a set of larger fusion proteins (*e.g.*, for phage display) containing the set of PDGFD sequences therein. There are a variety of methods which can be used to produce libraries of potential PDGFD variants from a degenerate oligonucleotide sequence. Chemical synthesis of a degenerate gene sequence can be performed in an automatic DNA synthesizer, and the synthetic gene then ligated into an appropriate expression vector. Use of a degenerate set of genes allows for the provision, in one mixture, of all of the sequences encoding the desired set of potential PDGFD variant sequences. Methods for synthesizing degenerate oligonucleotides are known in the art (see, *e.g.*, Narang (1983) *Tetrahedron* 39:3; Itakura *et al.* (1984) *Annu Rev Biochem* 53:323; Itakura *et al.* (1984) *Science* 198:1056; Ike *et al.* (1983) *Nucl Acid Res* 11:477.

Definitions

Unless otherwise defined, scientific and technical terms used in connection with the present invention shall have the meanings that are commonly understood by those of ordinary skill in the art. Further, unless otherwise required by context, singular terms shall include pluralities and plural terms shall include the singular. Generally, nomenclatures utilized in connection with, and techniques of, cell and tissue culture, molecular biology, and protein and oligo- or polynucleotide chemistry and

hybridization described herein are those well known and commonly used in the art. Standard techniques are used for recombinant DNA, oligonucleotide synthesis, and tissue culture and transformation (e.g., electroporation, lipofection). Enzymatic reactions and purification techniques are performed according to manufacturer's specifications or as commonly accomplished in the art or as described herein. The foregoing techniques and procedures are generally performed according to conventional methods well known in the art and as described in various general and more specific references that are cited and discussed throughout the present specification. *See e.g.*, Sambrook et al. *Molecular Cloning: A Laboratory Manual* (2d ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. (1989)). The nomenclatures utilized in connection with, and the laboratory procedures and techniques of, analytical chemistry, synthetic organic chemistry, and medicinal and pharmaceutical chemistry described herein are those well known and commonly used in the art. Standard techniques are used for chemical syntheses, chemical analyses, pharmaceutical preparation, formulation, and delivery, and treatment of patients.

As utilized in accordance with the present disclosure, the following terms, unless otherwise indicated, shall be understood to have the following meanings:

The term "isolated polynucleotide" as used herein shall mean a polynucleotide of genomic, cDNA, or synthetic origin or some combination thereof, which by virtue of its origin the "isolated polynucleotide" (1) is not associated with all or a portion of a polynucleotide in which the "isolated polynucleotide" is found in nature, (2) is operably linked to a polynucleotide which it is not linked to in nature, or (3) does not occur in nature as part of a larger sequence.

The term "isolated protein" referred to herein means a protein of cDNA, recombinant RNA, or synthetic origin or some combination thereof, which by virtue of its origin, or source of derivation, the "isolated protein" (1) is not associated with proteins found in nature, (2) is free of other proteins from the same source, e.g. free of murine proteins, (3) is expressed by a cell from a different species, or (4) does not occur in nature.

The term "polypeptide" is used herein as a generic term to refer to native protein, fragments, or analogs of a polypeptide sequence. Hence, native protein, fragments, and analogs are species of the polypeptide genus. Preferred polypeptides in accordance with the invention comprise the human heavy chain immunoglobulin molecules represented by Figures 1, 5, 9, 13, 17, 21, 25, and 29 and the human kappa light chain immunoglobulin molecules represented by Figures 3, 7, 11, 15, 19, 23, 27, and 31, as well as antibody molecules formed by combinations comprising the heavy chain immunoglobulin molecules with light chain immunoglobulin molecules, such as the kappa light chain immunoglobulin molecules, and vice versa, as well as fragments and analogs thereof.

The term "naturally-occurring" as used herein as applied to an object refers to the fact that an object can be found in nature. For example, a polypeptide or polynucleotide sequence that is present

in an organism (including viruses) that can be isolated from a source in nature and which has not been intentionally modified by man in the laboratory or otherwise is naturally-occurring.

The term "operably linked" as used herein refers to positions of components so described are in a relationship permitting them to function in their intended manner. A control sequence "operably linked" to a coding sequence is ligated in such a way that expression of the coding sequence is achieved under conditions compatible with the control sequences.

The term "control sequence" as used herein refers to polynucleotide sequences which are necessary to effect the expression and processing of coding sequences to which they are ligated. The nature of such control sequences differs depending upon the host organism; in prokaryotes, such control sequences generally include promoter, ribosomal binding site, and transcription termination sequence; in eukaryotes, generally, such control sequences include promoters and transcription termination sequence. The term "control sequences" is intended to include, at a minimum, all components whose presence is essential for expression and processing, and can also include additional components whose presence is advantageous, for example, leader sequences and fusion partner sequences.

The term "polynucleotide" as referred to herein means a polymeric form of nucleotides of at least 10 bases in length, either ribonucleotides or deoxynucleotides or a modified form of either type of nucleotide. The term includes single and double stranded forms of DNA.

The term "oligonucleotide" referred to herein includes naturally occurring, and modified nucleotides linked together by naturally occurring, and non-naturally occurring oligonucleotide linkages. Oligonucleotides are a polynucleotide subset generally comprising a length of 200 bases or fewer. Preferably oligonucleotides are 10 to 60 bases in length and most preferably 12, 13, 14, 15, 16, 17, 18, 19, or 20 to 40 bases in length. Oligonucleotides are usually single stranded, e.g. for probes; although oligonucleotides may be double stranded, e.g. for use in the construction of a gene mutant. Oligonucleotides of the invention can be either sense or antisense oligonucleotides.

The term "naturally occurring nucleotides" referred to herein includes deoxyribonucleotides and ribonucleotides. The term "modified nucleotides" referred to herein includes nucleotides with modified or substituted sugar groups and the like. The term "oligonucleotide linkages" referred to herein includes oligonucleotides linkages such as phosphorothioate, phosphorodithioate, phosphoroselenoate, phosphorodiselenoate, phosphoroanilothioate, phoshoraniladate, phosphoroamidate, and the like. *See e.g.,* LaPlanche et al. *Nucl. Acids Res.* **14**:9081 (1986); Stec et al. *J. Am. Chem. Soc.* **106**:6077 (1984); Stein et al. *Nucl. Acids Res.* **16**:3209 (1988); Zon et al. *Anti-Cancer Drug Design* **6**:539 (1991); Zon et al. *Oligonucleotides and Analogues: A Practical Approach*, pp. 87-108 (F. Eckstein, Ed., Oxford University Press, Oxford England (1991)); Stec et al. U.S. Patent No. 5,151,510; Uhlmann and Peyman *Chemical Reviews* **90**:543 (1990). An oligonucleotide can include a label for detection, if desired.

The term "selectively hybridize" referred to herein means to detectably and specifically bind. Polynucleotides, oligonucleotides and fragments thereof in accordance with the invention selectively hybridize to nucleic acid strands under hybridization and wash conditions that minimize appreciable amounts of detectable binding to nonspecific nucleic acids. High stringency conditions can be used to achieve selective hybridization conditions as known in the art and discussed herein. Generally, the nucleic acid sequence homology between the polynucleotides, oligonucleotides, and fragments of the invention and a nucleic acid sequence of interest will be at least 80%, and more typically with preferably increasing homologies of at least 85%, 90%, 95%, 99%, and 100%. Two amino acid sequences are homologous if there is a partial or complete identity between their sequences. For example, 85% homology means that 85% of the amino acids are identical when the two sequences are aligned for maximum matching. Gaps (in either of the two sequences being matched) are allowed in maximizing matching; gap lengths of 5 or less are preferred with 2 or less being more preferred. Alternatively and preferably, two protein sequences (or polypeptide sequences derived from them of at least 30 amino acids in length) are homologous, as this term is used herein, if they have an alignment score of at more than 5 (in standard deviation units) using the program ALIGN with the mutation data matrix and a gap penalty of 6 or greater. *See* Dayhoff, M.O., in *Atlas of Protein Sequence and Structure*, pp. 101-110 (Volume 5, National Biomedical Research Foundation (1972)) and Supplement 2 to this volume, pp. 1-10. The two sequences or parts thereof are more preferably homologous if their amino acids are greater than or equal to 50% identical when optimally aligned using the ALIGN program. The term "corresponds to" is used herein to mean that a polynucleotide sequence is homologous (i.e., is identical, not strictly evolutionarily related) to all or a portion of a reference polynucleotide sequence, or that a polypeptide sequence is identical to a reference polypeptide sequence. In contradistinction, the term "complementary to" is used herein to mean that the complementary sequence is homologous to all or a portion of a reference polynucleotide sequence. For illustration, the nucleotide sequence "TATAC" corresponds to a reference sequence "TATAC" and is complementary to a reference sequence "GTATA".

The following terms are used to describe the sequence relationships between two or more polynucleotide or amino acid sequences: "reference sequence", "comparison window", "sequence identity", "percentage of sequence identity", and "substantial identity". A "reference sequence" is a defined sequence used as a basis for a sequence comparison; a reference sequence may be a subset of a larger sequence, for example, as a segment of a full-length cDNA or gene sequence given in a sequence listing or may comprise a complete cDNA or gene sequence. Generally, a reference sequence is at least 18 nucleotides or 6 amino acids in length, frequently at least 24 nucleotides or 8 amino acids in length, and often at least 48 nucleotides or 16 amino acids in length. Since two polynucleotides or amino acid sequences may each (1) comprise a sequence (i.e., a portion of the complete polynucleotide or amino acid sequence) that is similar between the two molecules, and (2)

may further comprise a sequence that is divergent between the two polynucleotides or amino acid sequences, sequence comparisons between two (or more) molecules are typically performed by comparing sequences of the two molecules over a "comparison window" to identify and compare local regions of sequence similarity. A "comparison window", as used herein, refers to a conceptual segment of at least 18 contiguous nucleotide positions or 6 amino acids wherein a polynucleotide sequence or amino acid sequence may be compared to a reference sequence of at least 18 contiguous nucleotides or 6 amino acid sequences and wherein the portion of the polynucleotide sequence in the comparison window may comprise additions, deletions, substitutions, and the like (i.e., gaps) of 20 percent or less as compared to the reference sequence (which does not comprise additions or deletions) for optimal alignment of the two sequences. Optimal alignment of sequences for aligning a comparison window may be conducted by the local homology algorithm of Smith and Waterman *Adv. Appl. Math.* 2:482 (1981), by the homology alignment algorithm of Needleman and Wunsch *J. Mol. Biol.* 48:443 (1970), by the search for similarity method of Pearson and Lipman *Proc. Natl. Acad. Sci. (U.S.A.)* 85:2444 (1988), by computerized implementations of these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package Release 7.0, (Genetics Computer Group, 575 Science Dr., Madison, Wis.), Geneworks, or MacVector software packages), or by inspection, and the best alignment (i.e., resulting in the highest percentage of homology over the comparison window) generated by the various methods is selected.

The term "sequence identity" means that two polynucleotide or amino acid sequences are identical (i.e., on a nucleotide-by-nucleotide or residue-by-residue basis) over the comparison window. The term "percentage of sequence identity" is calculated by comparing two optimally aligned sequences over the window of comparison, determining the number of positions at which the identical nucleic acid base (e.g., A, T, C, G, U, or I) or residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the comparison window (i.e., the window size), and multiplying the result by 100 to yield the percentage of sequence identity. The terms "substantial identity" as used herein denotes a characteristic of a polynucleotide or amino acid sequence, wherein the polynucleotide or amino acid comprises a sequence that has at least 85 percent sequence identity, preferably at least 90 to 95 percent sequence identity, more usually at least 99 percent sequence identity as compared to a reference sequence over a comparison window of at least 18 nucleotide (6 amino acid) positions, frequently over a window of at least 24-48 nucleotide (8-16 amino acid) positions, wherein the percentage of sequence identity is calculated by comparing the reference sequence to the sequence which may include deletions or additions which total 20 percent or less of the reference sequence over the comparison window. The reference sequence may be a subset of a larger sequence.

As used herein, the twenty conventional amino acids and their abbreviations follow conventional usage. *See Immunology - A Synthesis* (2nd Edition, E.S. Golub and D.R. Gren, Eds.,

Sinauer Associates, Sunderland, Mass. (1991)). Stereoisomers (e.g., D-amino acids) of the twenty conventional amino acids, unnatural amino acids such as α-, α-disubstituted amino acids, N-alkyl amino acids, lactic acid, and other unconventional amino acids may also be suitable components for polypeptides of the present invention. Examples of unconventional amino acids include: 4-hydroxyproline, γ -carboxyglutamate, ε-N,N,N-trimethyllysine, ε-N-acetyllysine, O-phosphoserine, N-acetylserine, N-formylmethionine, 3-methylhistidine, 5-hydroxylysine, σ-N-methylarginine, and other similar amino acids and imino acids (e.g., 4-hydroxyproline). In the polypeptide notation used herein, the lefthand direction is the amino terminal direction and the righthand direction is the carboxy-terminal direction, in accordance with standard usage and convention.

Similarly, unless specified otherwise, the lefthand end of single-stranded polynucleotide sequences is the 5' end; the lefthand direction of double-stranded polynucleotide sequences is referred to as the 5' direction. The direction of 5' to 3' addition of nascent RNA transcripts is referred to as the transcription direction; sequence regions on the DNA strand having the same sequence as the RNA and which are 5' to the 5' end of the RNA transcript are referred to as "upstream sequences"; sequence regions on the DNA strand having the same sequence as the RNA and which are 3' to the 3' end of the RNA transcript are referred to as "downstream sequences".

As applied to polypeptides, the term "substantial identity" means that two peptide sequences, when optimally aligned, such as by the programs GAP or BESTFIT using default gap weights, share at least 80 percent sequence identity, preferably at least 90 percent sequence identity, more preferably at least 95 percent sequence identity, and most preferably at least 99 percent sequence identity. Preferably, residue positions which are not identical differ by conservative amino acid substitutions. Conservative amino acid substitutions refer to the interchangeability of residues having similar side chains. For example, a group of amino acids having aliphatic side chains is glycine, alanine, valine, leucine, and isoleucine; a group of amino acids having aliphatic-hydroxyl side chains is serine and threonine; a group of amino acids having amide-containing side chains is asparagine and glutamine; a group of amino acids having aromatic side chains is phenylalanine, tyrosine, and tryptophan; a group of amino acids having basic side chains is lysine, arginine, and histidine; and a group of amino acids having sulfur-containing side chains is cysteine and methionine. Preferred conservative amino acids substitution groups are: valine-leucine-isoleucine, phenylalanine-tyrosine, lysine-arginine, alanine-valine, glutamic-aspartic, and asparagine-glutamine.

As discussed herein, minor variations in the amino acid sequences of antibodies or immunoglobulin molecules are contemplated as being encompassed by the present invention, providing that the variations in the amino acid sequence maintain at least 75%, more preferably at least 80%, 90%, 95%, and most preferably 99%. In particular, conservative amino acid replacements are contemplated. Conservative replacements are those that take place within a family of amino acids that are related in their side chains. Genetically encoded amino acids are generally divided into

families: (1) acidic=aspartate, glutamate; (2) basic=lysine, arginine, histidine; (3) non-polar=alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan; and (4) uncharged polar=glycine, asparagine, glutamine, cysteine, serine, threonine, tyrosine. More preferred families are: serine and threonine are aliphatic-hydroxy family; asparagine and glutamine are an amide-containing family; alanine, valine, leucine and isoleucine are an aliphatic family; and phenylalanine, tryptophan, and tyrosine are an aromatic family. For example, it is reasonable to expect that an isolated replacement of a leucine with an isoleucine or valine, an aspartate with a glutamate, a threonine with a serine, or a similar replacement of an amino acid with a structurally related amino acid will not have a major effect on the binding or properties of the resulting molecule, especially if the replacement does not involve an amino acid within a framework site. Whether an amino acid change results in a functional peptide can readily be determined by assaying the specific activity of the polypeptide derivative. Assays are described in detail herein. Fragments or analogs of antibodies or immunoglobulin molecules can be readily prepared by those of ordinary skill in the art. Preferred amino- and carboxy-termini of fragments or analogs occur near boundaries of functional domains. Structural and functional domains can be identified by comparison of the nucleotide and/or amino acid sequence data to public or proprietary sequence databases. Preferably, computerized comparison methods are used to identify sequence motifs or predicted protein conformation domains that occur in other proteins of known structure and/or function. Methods to identify protein sequences that fold into a known three-dimensional structure are known. Bowie et al. *Science* **253**:164 (1991). Thus, the foregoing examples demonstrate that those of skill in the art can recognize sequence motifs and structural conformations that may be used to define structural and functional domains in accordance with the invention.

Preferred amino acid substitutions are those which: (1) reduce susceptibility to proteolysis, (2) reduce susceptibility to oxidation, (3) alter binding affinity for forming protein complexes, (4) alter binding affinities, and (4) confer or modify other physicochemical or functional properties of such analogs. Analogs can include various muteins of a sequence other than the naturally-occurring peptide sequence. For example, single or multiple amino acid substitutions (preferably conservative amino acid substitutions) may be made in the naturally-occurring sequence (preferably in the portion of the polypeptide outside the domain(s) forming intermolecular contacts. A conservative amino acid substitution should not substantially change the structural characteristics of the parent sequence (e.g., a replacement amino acid should not tend to break a helix that occurs in the parent sequence, or disrupt other types of secondary structure that characterizes the parent sequence). Examples of art-recognized polypeptide secondary and tertiary structures are described in *Proteins, Structures and Molecular Principles* (Creighton, Ed., W. H. Freeman and Company, New York (1984)); *Introduction to Protein Structure* (C. Branden and J. Tooze, eds., Garland Publishing, New York, N.Y. (1991)); and Thornton et at. *Nature* **354**:105 (1991).

The term "polypeptide fragment" as used herein refers to a polypeptide that has an amino-terminal and/or carboxy-terminal deletion, but where the remaining amino acid sequence is identical to the corresponding positions in the naturally-occurring sequence deduced, for example, from a full-length cDNA sequence. Fragments typically are at least 5, 6, 8 or 10 amino acids long, preferably at least 14 amino acids long, more preferably at least 20 amino acids long, usually at least 50 amino acids long, and even more preferably at least 70 amino acids long. The term "analog" as used herein refers to polypeptides which are comprised of a segment of at least 25 amino acids that has substantial identity to a portion of a deduced amino acid sequence and which has at least one of the following properties: (1) specific binding to a PDGFD, under suitable binding conditions, (2) ability to block appropriate PDGFD binding, or (3) ability to inhibit PDGFD expressing cell growth *in vitro* or *in vivo*. Typically, polypeptide analogs comprise a conservative amino acid substitution (or addition or deletion) with respect to the naturally-occurring sequence. Analogs typically are at least 20 amino acids long, preferably at least 50 amino acids long or longer, and can often be as long as a full-length naturally-occurring polypeptide.

Peptide analogs are commonly used in the pharmaceutical industry as non-peptide drus with properties analogous to those of the template peptide. These types of non-peptide compound are termed "peptide mimetics" or "peptidomimetics". Fauchere, *J. Adv. Drug Res.* 15:29 (1986); Veber and Freidinger *TINS* p.392 (1985); and Evans et al. *J. Med. Chem.* 30:1229 (1987). Such compounds are often developed with the aid of computerized molecular modeling. Peptide mimetics that are structurally similar to therapeutically useful peptides may be used to produce an equivalent therapeutic or prophylactic effect. Generally, peptidomimetics are structurally similar to a paradigm polypeptide (i.e., a polypeptide that has a biochemical property or pharmacological activity), such as human antibody, but have one or more peptide linkages optionally replaced by a linkage selected from the group consisting of: $--CH_2NH--$, $--CH_2S--$, $--CH_2-CH_2--$, --CH=CH--(cis and trans), $--COCH_2--$, $--CH(OH)CH_2--$, and $--CH_2SO--$, by methods well known in the art. Systematic substitution of one or more amino acids of a consensus sequence with a D-amino acid of the same type (e.g., D-lysine in place of L-lysine) may be used to generate more stable peptides. In addition, constrained peptides comprising a consensus sequence or a substantially identical consensus sequence variation may be generated by methods known in the art (Rizo and Gierasch *Ann. Rev. Biochem.* 61:387 (1992)); for example, by adding internal cysteine residues capable of forming intramolecular disulfide bridges which cyclize the peptide.

"Antibody" or "antibody peptide(s)" refer to an intact antibody, or a binding fragment thereof that competes with the intact antibody for specific binding. Binding fragments are produced by recombinant DNA techniques, or by enzymatic or chemical cleavage of intact antibodies. Binding fragments include Fab, Fab', $F(ab')_2$, Fv, and single-chain antibodies. An antibody other than a "bispecific" or "bifunctional" antibody is understood to have each of its binding sites identical. An

antibody substantially inhibits adhesion of a receptor to a counterreceptor when an excess of antibody reduces the quantity of receptor bound to counterreceptor by at least about 20%, 40%, 60% or 80%, and more usually greater than about 85% (as measured in an *in vitro* competitive binding assay).

The term "epitope" includes any protein determinant capable of specific binding to an immunoglobulin or T-cell receptor. Epitopic determinants usually consist of chemically active surface groupings of molecules such as amino acids or sugar side chains and usually have specific three dimensional structural characteristics, as well as specific charge characteristics. An antibody is said to specifically bind an antigen when the dissociation constant is ≤ 1 μM, preferably ≤ 100 nM and most preferably ≤ 10 nM.

The term "agent" is used herein to denote a chemical compound, a mixture of chemical compounds, a biological macromolecule, or an extract made from biological materials.

As used herein, the terms "label" or "labeled" refers to incorporation of a detectable marker, e.g., by incorporation of a radiolabeled amino acid or attachment to a polypeptide of biotinyl moieties that can be detected by marked avidin (e.g., streptavidin containing a fluorescent marker or enzymatic activity that can be detected by optical or colorimetric methods). In certain situations, the label or marker can also be therapeutic. Various methods of labeling polypeptides and glycoproteins are known in the art and may be used. Examples of labels for polypeptides include, but are not limited to, the following: radioisotopes or radionuclides (*e.g.*, ^{3}H, ^{14}C, ^{15}N, ^{35}S, ^{90}Y, ^{99}Tc, ^{111}In, ^{125}I, ^{131}I), fluorescent labels (*e.g.*, FITC, rhodamine, lanthanide phosphors), enzymatic labels (*e.g.*, horseradish peroxidase, β-galactosidase, luciferase, alkaline phosphatase), chemiluminescent, biotinyl groups, predetermined polypeptide epitopes recognized by a secondary reporter (e.g., leucine zipper pair sequences, binding sites for secondary antibodies, metal binding domains, epitope tags). In some embodiments, labels are attached by spacer arms of various lengths to reduce potential steric hindrance.

The term "pharmaceutical agent or drug" as used herein refers to a chemical compound or composition capable of inducing a desired therapeutic effect when properly administered to a patient. Other chemistry terms herein are used according to conventional usage in the art, as exemplified by *The McGraw-Hill Dictionary of Chemical Terms* (Parker, S., Ed., McGraw-Hill, San Francisco (1985))).

The term "antineoplastic agent" is used herein to refer to agents that have the functional property of inhibiting a development or progression of a neoplasm in a human, particularly a malignant (cancerous) lesion, such as a carcinoma, sarcoma, lymphoma, or leukemia. Inhibition of metastasis is frequently a property of antineoplastic agents.

As used herein, "substantially pure" means an object species is the predominant species present (i.e., on a molar basis it is more abundant than any other individual species in the composition), and preferably a substantially purified fraction is a composition wherein the object

species comprises at least about 50 percent (on a molar basis) of all macromolecular species present. Generally, a substantially pure composition will comprise more than about 80 percent of all macromolecular species present in the composition, more preferably more than about 85%, 90%, 95%, and 99%. Most preferably, the object species is purified to essential homogeneity (contaminant species cannot be detected in the composition by conventional detection methods) wherein the composition consists essentially of a single macromolecular species.

The term patient includes human and veterinary subjects.

Antibody Structure

The basic antibody structural unit is known to comprise a tetramer. Each tetramer is composed of two identical pairs of polypeptide chains, each pair having one "light" (about 25 kDa) and one "heavy" chain (about 50-70 kDa). The amino-terminal portion of each chain includes a variable region of about 100 to 110 or more amino acids primarily responsible for antigen recognition. The carboxy-terminal portion of each chain defines a constant region primarily responsible for effector function. Human light chains are classified as kappa and lambda light chains. Heavy chains are classified as mu, delta, gamma, alpha, or epsilon, and define the antibody's isotype as IgM, IgD, IgA, and IgE, respectively. Within light and heavy chains, the variable and constant regions are joined by a "J" region of about 12 or more amino acids, with the heavy chain also including a "D" region of about 10 more amino acids. *See generally, Fundamental Immunology* Ch. 7 (Paul, W., ed., 2nd ed. Raven Press, N.Y. (1989)). The variable regions of each light/heavy chain pair form the antibody binding site.

Thus, an intact antibody has two binding sites. Except in bifunctional or bispecific antibodies, the two binding sites are the same.

The chains all exhibit the same general structure of relatively conserved framework regions (FR) joined by three hyper variable regions, also called complementarity determining regions or CDRs. The CDRs from the two chains of each pair are aligned by the framework regions, enabling binding to a specific epitope. From N-terminal to C-terminal, both light and heavy chains comprise the domains FR1, CDR1, FR2, CDR2, FR3, CDR3 and FR4. The assignment of amino acids to each domain is in accordance with the definitions of Kabat *Sequences of Proteins of Immunological Interest* (National Institutes of Health, Bethesda, Md. (1987 and 1991)), or Chothia & Lesk *J. Mol. Biol.* **196**:901-917 (1987); Chothia et al. *Nature* **342**:878-883 (1989).

A bispecific or bifunctional antibody is an artificial hybrid antibody having two different heavy/light chain pairs and two different binding sites. Bispecific antibodies can be produced by a variety of methods including fusion of hybridomas or linking of Fab' fragments. *See, e.g.,* Songsivilai & Lachmann *Clin. Exp. Immunol.* **79**: 315-321 (1990), Kostelny et al. *J. Immunol.* **148**:1547-1553 (1992). Production of bispecific antibodies can be a relatively labor intensive process compared with production of conventional antibodies and yields and degree of purity are generally lower for

bispecific antibodies. Bispecific antibodies do not exist in the form of fragments having a single binding site (e.g., Fab, Fab', and Fv).

Human Antibodies and Humanization of Antibodies

Human antibodies avoid certain of the problems associated with antibodies that possess murine or rat variable and/or constant regions. The presence of such murine or rat derived proteins can lead to the rapid clearance of the antibodies or can lead to the generation of an immune response against the antibody by a patient. In order to avoid the utilization of murine or rat derived antibodies, it has been postulated that one can develop humanized antibodies or generate fully human antibodies through the introduction of human antibody function into a rodent so that the rodent would produce fully human antibodies.

Human Antibodies

The ability to clone and reconstruct megabase-sized human loci in YACs and to introduce them into the mouse germline provides a powerful approach to elucidating the functional components of very large or crudely mapped loci as well as generating useful models of human disease. Furthermore, the utilization of such technology for substitution of mouse loci with their human equivalents could provide unique insights into the expression and regulation of human gene products during development, their communication with other systems, and their involvement in disease induction and progression.

An important practical application of such a strategy is the "humanization" of the mouse humoral immune system. Introduction of human immunoglobulin (Ig) loci into mice in which the endogenous Ig genes have been inactivated offers the opportunity to study the mechanisms underlying programmed expression and assembly of antibodies as well as their role in B-cell development. Furthermore, such a strategy could provide an ideal source for production of fully human monoclonal antibodies (Mabs) - an important milestone towards fulfilling the promise of antibody therapy in human disease. Fully human antibodies are expected to minimize the immunogenic and allergic responses intrinsic to mouse or mouse-derivatized Mabs and thus to increase the efficacy and safety of the administered antibodies. The use of fully human antibodies can be expected to provide a substantial advantage in the treatment of chronic and recurring human diseases, such as inflammation, autoimmunity, and cancer, which require repeated antibody administrations.

One approach towards this goal was to engineer mouse strains deficient in mouse antibody production with large fragments of the human Ig loci in anticipation that such mice would produce a large repertoire of human antibodies in the absence of mouse antibodies. Large human Ig fragments would preserve the large variable gene diversity as well as the proper regulation of antibody production and expression. By exploiting the mouse machinery for antibody diversification and selection and the lack of immunological tolerance to human proteins, the reproduced human antibody repertoire in these mouse strains should yield high affinity antibodies against any antigen of interest,

including human antigens. Using the hybridoma technology, antigen-specific human Mabs with the desired specificity could be readily produced and selected.

This general strategy was demonstrated in connection with our generation of the first XenoMouse™ strains as published in 1994. *See* Green et al. *Nature Genetics* 7:13-21 (1994). The XenoMouse™ strains were engineered with yeast artificial chromosomes (YACs) containing 245 kb and 190 kb-sized germline configuration fragments of the human heavy chain locus and kappa light chain locus, respectively, which contained core variable and constant region sequences. *Id.* The human Ig containing YACs proved to be compatible with the mouse system for both rearrangement and expression of antibodies and were capable of substituting for the inactivated mouse Ig genes. This was demonstrated by their ability to induce B-cell development, to produce an adult-like human repertoire of fully human antibodies, and to generate antigen-specific human Mabs. These results also suggested that introduction of larger portions of the human Ig loci containing greater numbers of V genes, additional regulatory elements, and human Ig constant regions might recapitulate substantially the full repertoire that is characteristic of the human humoral response to infection and immunization. The work of Green et al. was recently extended to the introduction of greater than approximately 80% of the human antibody repertoire through introduction of megabase sized, germline configuration YAC fragments of the human heavy chain loci and kappa light chain loci, respectively, to produce XenoMouse™ mice. *See* Mendez et al. *Nature Genetics* 15:146-156 (1997) and U.S. Patent Application Serial No. 08/759,620, filed December 3, 1996.

Such approach is further discussed and delineated in U.S. Patent Application Serial Nos. 07/466,008, filed January 12, 1990, 07/610,515, filed November 8, 1990, 07/919,297, filed July 24, 1992, 07/922,649, filed July 30, 1992, filed 08/031,801, filed March 15,1993, 08/112,848, filed August 27, 1993, 08/234,145, filed April 28, 1994, 08/376,279, filed January 20, 1995, 08/430, 938, April 27, 1995, 08/464,584, filed June 5, 1995, 08/464,582, filed June 5, 1995, 08/463,191, filed June 5, 1995, 08/462,837, filed June 5, 1995, 08/486,853, filed June 5, 1995, 08/486,857, filed June 5, 1995, 08/486,859, filed June 5, 1995, 08/462,513, filed June 5, 1995, 08/724,752, filed October 2, 1996, and 08/759,620, filed December 3, 1996 and U.S. Patent Nos. 6,162,963, 6,150,584, 6,114,598, 6,075,181, and 5,939,598 and Japanese Patent Nos. 3 068 180 B2, 3 068 506 B2, and 3 068 507 B2. *See also* Mendez et al. *Nature Genetics* 15:146-156 (1997) and Green and Jakobovits *J. Exp. Med.* 188:483-495 (1998). *See also* European Patent No., EP 0 463 151 B1, grant published June 12, 1996, International Patent Application No., WO 94/02602, published February 3, 1994, International Patent Application No., WO 96/34096, published October 31, 1996, WO 98/24893, published June 11, 1998, WO 00/76310, published December 21, 2000.

In an alternative approach, others, including GenPharm International, Inc., have utilized a "minilocus" approach. In the minilocus approach, an exogenous Ig locus is mimicked through the inclusion of pieces (individual genes) from the Ig locus. Thus, one or more V_H genes, one or more D_H

genes, one or more J_H genes, a mu constant region, and a second constant region (preferably a gamma constant region) are formed into a construct for insertion into an animal. This approach is described in U.S. Patent No. 5,545,807 to Surani et al. and U.S. Patent Nos. 5,545,806, 5,625,825, 5,625,126, 5,633,425, 5,661,016, 5,770,429, 5,789,650, 5,814,318, 5,877,397, 5,874,299, and 6,255,458 each to Lonberg and Kay, U.S. Patent No. 5,591,669 and 6,023.010 to Krimpenfort and Berns, U.S. Patent Nos. 5,612,205, 5,721,367, and 5,789,215 to Berns et al., and U.S. Patent No. 5,643,763 to Choi and Dunn, and GenPharm International U.S. Patent Application Serial Nos. 07/574,748, filed August 29, 1990, 07/575,962, filed August 31, 1990, 07/810,279, filed December 17, 1991, 07/853,408, filed March 18, 1992, 07/904,068, filed June 23, 1992, 07/990,860, filed December 16, 1992, 08/053,131, filed April 26, 1993, 08/096,762, filed July 22, 1993, 08/155,301, filed November 18, 1993, 08/161,739, filed December 3, 1993, 08/165,699, filed December 10, 1993, 08/209,741, filed March 9, 1994. *See also* European Patent No. 0 546 073 B1, International Patent Application Nos. WO 92/03918, WO 92/22645, WO 92/22647, WO 92/22670, WO 93/12227, WO 94/00569, WO 94/25585, WO 96/14436, WO 97/13852, and WO 98/24884 and U.S. Patent No. 5,981,175. *See further* Taylor et al., 1992, Chen et al., 1993, Tuaillon et al., 1993, Choi et al., 1993, Lonberg et al., (1994), Taylor et al., (1994), and Tuaillon et al., (1995), Fishwild et al., (1996).

The inventors of Surani et al., cited above and assigned to the Medical Research Counsel (the "MRC"), produced a transgenic mouse possessing an Ig locus through use of the minilocus approach. The inventors on the GenPharm International work, cited above, Lonberg and Kay, following the lead of the present inventors, proposed inactivation of the endogenous mouse Ig locus coupled with substantial duplication of the Surani et al. work.

An advantage of the minilocus approach is the rapidity with which constructs including portions of the Ig locus can be generated and introduced into animals. Commensurately, however, a significant disadvantage of the minilocus approach is that, in theory, insufficient diversity is introduced through the inclusion of small numbers of V, D, and J genes. Indeed, the published work appears to support this concern. B-cell development and antibody production of animals produced through use of the minilocus approach appear stunted. Therefore, research surrounding the present invention has consistently been directed towards the introduction of large portions of the Ig locus in order to achieve greater diversity and in an effort to reconstitute the immune repertoire of the animals.

Kirin has also demonstrated the generation of human antibodies from mice in which, through microcell fusion, large pieces of chromosomes, or entire chromosomes, have been introduced. *See* European Patent Application Nos. 773 288 and 843 961.

Human anti-mouse antibody (HAMA) responses have led the industry to prepare chimeric or otherwise humanized antibodies. While chimeric antibodies have a human constant region and a murine variable region, it is expected that certain human anti-chimeric antibody (HACA) responses will be observed, particularly in chronic or multi-dose utilizations of the antibody. Thus, it would be

desirable to provide fully human antibodies against PDGFD in order to vitiate concerns and/or effects of HAMA or HACA response.

Humanization and Display Technologies

As was discussed above in connection with human antibody generation, there are advantages to producing antibodies with reduced immunogenicity. To a degree, this can be accomplished in connection with techniques of humanization and display techniques using appropriate libraries. It will be appreciated that murine antibodies or antibodies from other species can be humanized or primatized using techniques well known in the art. *See e.g.,* Winter and Harris *Immunol Today* 14:43-46 (1993) and Wright et al. *Crit, Reviews in Immunol.* 12125-168 (1992). The antibody of interest may be engineered by recombinant DNA techniques to substitute the CH1, CH2, CH3, hinge domains, and/or the framework domain with the corresponding human sequence (*see* WO 92/02190 and U.S. Patent Nos. 5,530,101, 5,585,089, 5,693,761, 5,693,792, 5,714,350, and 5,777,085). Also, the use of Ig cDNA for construction of chimeric immunoglobulin genes is known in the art (Liu et al. *P.N.A.S.* 84:3439 (1987) and *J.Immunol.*139:3521 (1987)). mRNA is isolated from a hybridoma or other cell producing the antibody and used to produce cDNA. The cDNA of interest may be amplified by the polymerase chain reaction using specific primers (U.S. Pat. Nos. 4,683,195 and 4,683,202). Alternatively, a library is made and screened to isolate the sequence of interest. The DNA sequence encoding the variable region of the antibody is then fused to human constant region sequences. The sequences of human constant regions genes may be found in Kabat et al. (1991) Sequences of Proteins of Immunological Interest, N.I.H. publication no. 91-3242. Human C region genes are readily available from known clones. The choice of isotype will be guided by the desired effector functions, such as complement fixation, or activity in antibody-dependent cellular cytotoxicity. Preferred isotypes are IgG1, IgG3 and IgG4. Either of the human light chain constant regions, kappa or lambda, may be used. The chimeric, humanized antibody is then expressed by conventional methods.

Antibody fragments, such as Fv, F(ab').sub.2 and Fab may be prepared by cleavage of the intact protein, e.g. by protease or chemical cleavage. Alternatively, a truncated gene is designed. For example, a chimeric gene encoding a portion of the $F(ab')_2$ fragment would include DNA sequences encoding the CH1 domain and hinge region of the H chain, followed by a translational stop codon to yield the truncated molecule.

Consensus sequences of H and L J regions may be used to design oligonucleotides for use as primers to introduce useful restriction sites into the J region for subsequent linkage of V region segements to human C region segments. C region cDNA can be modified by site directed mutagenesis to place a restriction site at the analogous position in the human sequence.

Expression vectors include plasmids, retroviruses, YACs, EBV derived episomes, and the like. A convenient vector is one that encodes a functionally complete human CH or CL immunoglobulin sequence, with appropriate restriction sites engineered so that any VH or VL

sequence can be easily inserted and expressed. In such vectors, splicing usually occurs between the splice donor site in the inserted J region and the splice acceptor site preceding the human C region, and also at the splice regions that occur within the human CH exons. Polyadenylation and transcription termination occur at native chromosomal sites downstream of the coding regions. The resulting chimeric antibody may be joined to any strong promoter, including retroviral LTRs, e.g. SV-40 early promoter, (Okayama et al. *Mol. Cell. Bio.* 3:280 (1983)), Rous sarcoma virus LTR (Gorman et al. *P.N.A.S.* 79:6777 (1982)), and moloney murine leukemia virus LTR (Grosschedl et al. *Cell* 41:885 (1985)). Also, as will be appreciated, native Ig promoters and the like may be used.

Further, human antibodies or antibodies from other species can be generated through display-type technologies, including, without limitation, phage display, retroviral display, ribosomal display, and other techniques, using techniques well known in the art and the resulting molecules can be subjected to additional maturation, such as affinity maturation, as such techniques are well known in the art. Wright and Harris, *supra.*, Hanes and Plucthau *PNAS USA* 94:4937-4942 (1997) (ribosomal display), Parmley and Smith *Gene* 73:305-318 (1988) (phage display), Scott *TIBS* 17:241-245 (1992), Cwirla et al. *PNAS USA* 87:6378-6382 (1990), Russel et al. *Nucl. Acids Research* 21:1081-1085 (1993), Hoganboom et al. *Immunol. Reviews* 130:43-68 (1992), Chiswell and McCafferty *TIBTECH* 10:80-84 (1992), and U.S. Patent No. 5,733,743. If display technologies are utilized to produce antibodies that are not human, such antibodies can be humanized as described above.

Using these techniques, antibodies can be generated to PDGFD expressing cells, PDGFD itself, forms of PDGFD, epitopes or peptides thereof, and expression libraries thereto (*see e.g.* U.S. Patent No. 5,703,057) which can thereafter be screened as described above for the activities described above.

Additional Criteria for Antibody Therapeutics

As discussed herein, the function of the PDGFD antibody appears important to at least a portion of its mode of operation. By function, we mean, by way of example, the activity of the PDGFD antibody in operation PDGFD. Accordingly, in certain respects, it may be desirable in connection with the generation of antibodies as therapeutic candidates against PDGFD that the antibodies be capable of fixing complement and participating in CDC. There are a number of isotypes of antibodies that are capable of the same, including, without limitation, the following: murine IgM, murine IgG2a, murine IgG2b, murine IgG3, human IgM, human IgG1, and human IgG3. It will be appreciated that antibodies that are generated need not initially possess such an isotype but, rather, the antibody as generated can possess any isotype and the antibody can be isotype switched thereafter using conventional techniques that are well known in the art. Such techniques include the use of direct recombinant techniques (*see e.g.*, U.S. Patent No. 4,816,397), cell-cell fusion techniques (*see e.g.*, U.S. Patent Nos. 5,916,771 and 6,207,418), among others.

In the cell-cell fusion technique, a myeloma or other cell line is prepared that possesses a heavy chain with any desired isotype and another myeloma or other cell line is prepared that possesses the light chain. Such cells can, thereafter, be fused and a cell line expressing an intact antibody can be isolated.

By way of example, the PDGFD antibody discussed herein is a human anti- PDGFD IgG2 antibody. If such antibody possessed desired binding to the PDGFD molecule, it could be readily isotype switched to generate a human IgM, human IgG1, or human IgG3 isotype, while still possessing the same variable region (which defines the antibody's specificity and some of its affinity). Such molecule would then be capable of fixing complement and participating in CDC.

Accordingly, as antibody candidates are generated that meet desired "structural" attributes as discussed above, they can generally be provided with at least certain of the desired "functional" attributes through isotype switching.

Design and Generation of Other Therapeutics

In accordance with the present invention and based on the activity of the antibodies that are produced and characterized herein with respect to PDGFD, the design of other therapeutic modalities beyond antibody moieties is facilitated. Such modalities include, without limitation, advanced antibody therapeutics, such as bispecific antibodies, immunotoxins, and radiolabeled therapeutics, generation of peptide therapeutics, gene therapies, particularly intrabodies, antisense therapeutics, and small molecules.

In connection with the generation of advanced antibody therapeutics, where complement fixation is a desirable attribute, it may be possible to sidestep the dependence on complement for cell killing through the use of bispecifics, immunotoxins, or radiolabels, for example.

For example, in connection with bispecific antibodies, bispecific antibodies can be generated that comprise (i) two antibodies one with a specificity to PDGFD and another to a second molecule that are conjugated together, (ii) a single antibody that has one chain specific to PDGFD and a second chain specific to a second molecule, or (iii) a single chain antibody that has specificity to PDGFD and the other molecule. Such bispecific antibodies can be generated using techniques that are well known for example, in connection with (i) and (ii) *see e.g.,* Fanger et al. *Immunol Methods* 4:72-81 (1994) and Wright and Harris, *supra.* and in connection with (iii) *see e.g.,* Traunecker et al. *Int. J. Cancer (Suppl.)* 7:51-52 (1992). In each case, the second specificity can be made to the heavy chain activation receptors, including, without limitation, CD16 or CD64 (*see e.g.,* Deo et al. 18:127 (1997)) or CD89 (*see e.g.,* Valerius et al. *Blood* 90:4485-4492 (1997)). Bispecific antibodies prepared in accordance with the foregoing would be likely to kill cells expressing PDGFD, and particularly those cells in which the PDGFD antibodies of the invention are effective.

In connection with immunotoxins, antibodies can be modified to act as immunotoxins utilizing techniques that are well known in the art. *See e.g.,* Vitetta *Immunol Today* 14:252 (1993).

See also U.S. Patent No. 5,194,594. In connection with the preparation of radiolabeled antibodies, such modified antibodies can also be readily prepared utilizing techniques that are w ll known in the art. *See e.g.,* Junghans et al. in *Cancer Chemotherapy and Biotherapy* 655-686 (2d edition, Chafner and Longo, eds., Lippincott Raven (1996)). *See also* U.S. Patent Nos. 4,681,581, 4,735,210, 5,101,827, 5,102,990 (RE 35,500), 5,648,471, and 5,697,902. Each of immunotoxins and radiolabeled molecules would be likely to kill cells expressing PDGFD, and particularly those cells in which the antibodies of the invention are effective.

In connection with the generation of therapeutic peptides, through the utilization of structural information related to PDGFD and antibodies thereto, such as the antibodies of the invention (as discussed below in connection with small molecules) or screening of peptide libraries, therapeutic peptides can be generated that are directed against PDGFD. Design and screening of peptide therapeutics is discussed in connection with Houghten et al. *Biotechniques* 13:412-421 (1992), Houghten *PNAS USA* 82:5131-5135 (1985), Pinalla et al. *Biotechniques* 13:901-905 (1992), Blake and Litzi-Davis *BioConjugate Chem.* 3:510-513 (1992). Immunotoxins and radiolabeled molecules can also be prepared, and in a similar manner, in connection with peptidic moieties as discussed above in connection with antibodies.

Assuming that the PDGFD molecule (or a form, such as a splice variant or alternate form) is functionally active in a disease process, it will also be possible to design gene and antisense therapeutics thereto through conventional techniques. Such modalities can be utilized for modulating the function of PDGFD. In connection therewith the antibodies of the present invention facilitate design and use of functional assays related thereto. A design and strategy for antisense therapeutics is discussed in detail in International Patent Application No. WO 94/29444. Design and strategies for gene therapy are well known. However, in particular, the use of gene therapeutic techniques involving intrabodies could prove to be particularly advantageous. *See e.g.,* Chen et al. *Human Gene Therapy* 5:595-601 (1994) and Marasco *Gene Therapy* 4:11-15 (1997). General design of and considerations related to gene therapeutics is also discussed in International Patent Application No. WO 97/38137.

Small molecule therapeutics can also be envisioned in accordance with the present invention. Drugs can be designed to modulate the activity of PDGFD based upon the present invention. Knowledge gleaned from the structure of the PDGFD molecule and its interactions with other molecules in accordance with the present invention, such as the antibodies of the invention, and others can be utilized to rationally design additional therapeutic modalities. In this regard, rational drug design techniques such as X-ray crystallography, computer-aided (or assisted) molecular modeling (CAMM), quantitative or qualitative structure-activity relationship (QSAR), and similar technologies can be utilized to focus drug discovery efforts. Rational design allows prediction of protein or synthetic structures which can interact with the molecule or specific forms thereof which can be used

to modify or modulate the activity of PDGFD. Such structures can be synthesized chemically or expressed in biological systems. This approach has been reviewed in Capsey et al. *Genetically Engineered Human Therapeutic Drugs* (Stockton Press, NY (1988)). Further, combinatorial libraries can be designed and sythesized and used in screening programs, such as high throughput screening efforts.

Therapeutic Administration and Formulations

It will be appreciated that administration of therapeutic entities in accordance with the invention will be administered with suitable carriers, excipients, and other agents that are incorporated into formulations to provide improved transfer, delivery, tolerance, and the like. A multitude of appropriate formulations can be found in the formulary known to all pharmaceutical chemists: Remington's Pharmaceutical Sciences (15th ed, Mack Publishing Company, Easton, PA (1975)), particularly Chapter 87 by Blaug, Seymour, therein. These formulations include, for example, powders, pastes, ointments, jellies, waxes, oils, lipids, lipid (cationic or anionic) containing vesicles (such as Lipofectin™), DNA conjugates, anhydrous absorption pastes, oil-in-water and water-in-oil emulsions, emulsions carbowax (polyethylene glycols of various molecular weights), semi-solid gels, and semi-solid mixtures containing carbowax. Any of the foregoing mixtures may be appropriate in treatments and therapies in accordance with the present invention, provided that the active ingredient in the formulation is not inactivated by the formulation and the formulation is physiologically compatible and tolerable with the route of administration. *See also* Baldrick P. "Pharmaceutical excipient development: the need for preclinical guidance." *Regul. Toxicol. Pharmacol.* 32(2):210-8 (2000), Wang W. "Lyophilization and development of solid protein pharmaceuticals." *Int. J. Pharm.* 203(1-2):1-60 (2000), Charman WN "Lipids, lipophilic drugs, and oral drug delivery-some emerging concepts." *J Pharm Sci* .89(8):967-78 (2000), Powell et al. "Compendium of excipients for parenteral formulations" *PDA J Pharm Sci Technol.* 52:238-311 (1998) and the citations therein for additional information related to formulations, excipients and carriers well known to pharmaceutical chemists.

Preparation of Antibodies

Antibodies in accordance with the invention are preferably prepared through the utilization of a transgenic mouse that has a substantial portion of the human antibody producing genome inserted but that is rendered deficient in the production of endogenous, murine, antibodies. Such mice, then, are capable of producing human immunoglobulin molecules and antibodies and are deficient in the production of murine immunoglobulin molecules and antibodies. Technologies utilized for achieving the same are disclosed in the patents, applications, and references disclosed in the Background, herein. In particular, however, a preferred embodiment of transgenic production of mice and antibodies therefrom is disclosed in U.S. Patent Application Serial No. 08/759,620, filed December 3, 1996 and International Patent Application Nos. WO 98/24893, published June 11, 1998 and WO 00/76310, published December 21, 2000. *See also* Mendez et al. *Nature Genetics* **15**:146-156 (1997).

Through use of such technology, we have produced fully human monoclonal antibodies to a variety of antigens. Essentially, we immunize XenoMouse™ lines of mice with an antigen of interest, recover lymphatic cells (such as B-cells) from the mice that express antibodies, fuse such recovered cells with a myeloid-type cell line to prepare immortal hybridoma cell lines, and such hybridoma cell lines are screened and selected to identify hybridoma cell lines that produce antibodies specific to the antigen of interest. We utilized these techniques in accordance with the present invention for the preparation of antibodies specific to PDGFD. Herein, we describe the production of multiple hybridoma cell lines that produce antibodies specific to PDGFD. Further, we provide a characterization of the antibodies produced by such cell lines, including nucleotide and amino acid sequence analyses of the heavy and light chains of such antibodies.

The hybridoma cell lines discussed herein are designated 1.6.1, 1.11.1, 1.17.1, 1.18.1, 1.19.1, 1.23.1, 1.24, 1.25, 1.29, 1.33, 1.38, 1.39, 1.40, 1.45, 1.46, 1.48, 1.49, 1.51, and 6.4.1. Each of the antibodies produced by the aforementioned cell lines possess fully human IgG2 heavy chains with human kappa light chains. In general, antibodies in accordance with the invention possess high affinities, typically possessing Kd's of from about 10^{-6} through about 10^{-11} M, when measured by either solid phase and solution phase.

As will be appreciated, antibodies in accordance with the present invention can be expressed in cell lines other than hybridoma cell lines. Sequences encoding particular antibodies can be used for transformation of a suitable mammalian host cell. Transformation can be by any known method for introducing polynucleotides into a host cell, including, for example packaging the polynucleotide in a virus (or into a viral vector) and transducing a host cell with the virus (or vector) or by transfection procedures known in the art, as exemplified by U.S. Patent Nos. 4,399,216, 4,912,040, 4,740,461, and 4,959,455. The transformation procedure used depends upon the host to be transformed. Methods for introduction of heterologous polynucleotides into mammalian cells are well known in the art and include dextran-mediated transfection, calcium phosphate precipitation, polybrene mediated

transfection, protoplast fusion, electroporation, encapsulation of the polynucleotide(s) in liposomes, and direct microinjection of the DNA into nuclei.

Mammalian cell lines available as hosts for expression are well known in the art and include many immortalized cell lines available from the American Type Culture Collection (ATCC), including but not limited to Chinese hamster ovary (CHO) cells, HeLa cells, baby hamster kidney (BHK) cells, monkey kidney cells (COS), human hepatocellular carcinoma cells (e.g., Hep G2), and a number of other cell lines. Cell lines of particular preference are selected through determining which cell lines have high expression levels and produce antibodies with constitutive PDGFD binding properties.

Antibodies in accordance with the present invention are capable of binding to PDGFD. Further, antibodies of the invention are useful in the detection of PDGFD in patient samples and accordingly are useful as diagnostics as described hereinbelow. In addition, based on the potent inhibition of growth of fibroblast cells observed through use of antibodies of the invention, it is expected that such antibodies will have therapeutic effect in the treatment of malignant tissue growth and/or disease, such as cancer and obstructive tissue growths as discussed hereinbelow.

EXAMPLES

The following examples, including the experiments conducted and results achieved are provided for illustrative purposes only and are not to be construed as limiting upon the present invention.

EXAMPLE 1

Antibodies to PDGFD were generated as described in International Patent Application No. WO 01/25433 using an active protein fragment of the gene product from clone 30664188.0.99 arises in the conditioned medium obtained when HEK293 cells are transfected with the plasmid pCEP4/Sec-30664188 (see Examples 17 and 18). This vector harbors a fragment of the gene product of clone 30664188.0.99 that encompasses the entire amino acid sequence except for the predicted N-terminal signal peptide. The active fragment is termed the p35 form of the 30664188.0.99, or "p35" herein.

The active fragment p35 was employed as the immunogen to stimulate an immune response in XenoMouse® animals. Monoclonal antibodies directed against p35 were prepared by hybridoma technology from p35-immunized XenoMouse animals in standard fashion.

Several fully human monoclonal antibody clones were isolated from such immunizations and their ability to neutralize the growth promoting effects of the 30664188 p35 immunogen were analyzed using the BrdU incorporation assay on NIH 3T3 cells (described in International Patent Application No. WO 01/25433). The results for thirteen of the clones are presented in Table 1. An additional fully human monoclonal antibody, CURA2-1.17, was also identified that immunospecifically binds p35. In addition, ten other clones exhibited IC_{50} values >1000 ng/mL. Importantly, all of the monoclonal antibodies identified in this work had no inhibitory activity when

added with PDGF BB to the comparable BrdU incorporation assay, up to 1000 ng/mL. Thus the neutralizing fully human monoclonal antibodies identified wer specific for the p35 antigen.

In the BrdU assay, murine NIH 3T3 (ATCC No. CRL-1658, Manassas, VA) fibroblast cells were cultured in DMEM supplemented with 10% fetal bovine serum or 10% calf serum respectively. Fibroblasts were grown to confluence at 37°C in 10% CO_2/air. Cells were then starved in DMEM for 24 hours. Enriched conditioned medium was added (10 microL/100 microL of culture) for 18 h. BrdU (10 microM) was then added and incubated with the cells for 5 h. BrdU incorporation was assayed by colorimetric immunoassay according to the manufacturer's specifications (Boehringer Mannheim, Indianapolis, IN).

Figures 44-47 show BrdU incorporation assay results from experiments in which the neutralization of various human anti-PDGFD monoclonal antibodies of the invention was assessed. Figure 44 is a bar graphic representation comparing the levels of BrdU incorporation in NIH 3T3 cells upon exposure to various human anti-PDGFD monoclonal antibodies of the invention. Figures 45-47 are bar graphic representations comparing the levels of BrdU incorporation in NIH 3T3 cells upon exposure to various human anti-PDGFD monoclonal antibodies of the invention at varying doses as compared to a control run utilizing PDGFBB at varying concentrations.

TABLE 1

CURA2 MAb	IC_{50} (ng/mL)
1.6	75
1.9	100
1.18	>1000
1.19	75
1.22	100
1.29	150
1.35	1000
1.40	>1000
1.45	750
1.46	500
1.51	1000
1.59	500
6.4	75

EXAMPLE 2

An Enzyme-Linked Immunosorbent Assay (ELISA) for the detection of PDGFD Antigen in a Sample was developed. In the assay, wells of a microtiter plate, such as a 96-well microtiter plate or a 384-well microtiter plate, were adsorbed for several hours with a first fully human monoclonal antibody CURA2-1.6 (see Example 1) directed against the antigen. The immobilized CURA2-1.6

serves as a capture antibody for any of the antigen that may be present in a test sample. The wells were rinsed and treated with a blocking agent such as milk protein or albumin to prevent nonspecific adsorption of the analyte.

Subsequently the wells were treated with a test sample suspected of containing the antigen, or with a solution containing a standard amount of the antigen. Such a sample may be, for example, a serum sample from a subject suspected of having levels of circulating antigen considered to be diagnostic of a pathology.

After rinsing away the test sample or standard, the wells were treated with a second fully human monoclonal antibody CURA2-1.17 (see Example 1) that has been labeled by conjugation with biotin. The labeled CURA2-1.17 serves as a detecting antibody. After rinsing away excess second antibody, the wells were treated with avidin-conjugated horseradish peroxidase (HRP) and a suitable chromogenic substrate. The concentration of the antigen in the test samples was determined by comparison with a standard curve developed from the standard samples. The results obtained for such a standard curve are shown in Table 2.

This ELISA assay provides a highly specific and very sensitive assay for the antigen in a test sample.

TABLE 2

Two site, or sandwich, ELISA for the detection of a p35 antigen in a test sample.

PDGFD (ng/ml)

conc.nanog/ml	OD 490
1000	2.354
300	2.145
100	1.017
30	0.375
10	0.172
3	0.1
1	0.072

EXAMPLE 3

In order to determine the concentration of the PDGFD antigen in the serum of cancer patients, serum from human subjects diagnosed as suffering from various types of cancer, or as harboring various kinds of tumor, were obtained. In particular, serum from five patients suffering from cancer of the tongue, five patients suffering from Hodgkin's lymphoma, five patients suffering from prostate cancer, three patients suffering from lung cancer, four patients suffering from renal cancer, five patients suffering from melanoma and five patients suffering from myeloma were examined. The concentration of the antigen in the serum of these patients was assessed using an ELISA procedure

described in Example 2. The results are shown in Table 3. The results show that samples from 5 of the 5 tongue cancer patients contain high levels of th antigen, samples from 2 of 5 Hodgkin disease patients contain detectable amounts of the antigen (one of these at a high level), samples from 2 of 3 lung cancer patients contain detectable levels of antigen, a sample from 1 of 5 patients with prostate cancer contains a high level of the antigen, and a sample from 1 of 4 renal cancer patients contains a detectable concentration of the antigen. In addition to the results in Table 3, it was found that 1 of 5 patients with scleroderma has a low concentration of the antigen.

The results in this Example indicate that an immunoassay directed against circulating the antigen is a useful diagnostic procedure in the detection of certain cancers. The use of the assay in staging such cancers and in assessing a response to therapeutic treatment is also suggested by these results.

TABLE 3

Sera number	Designation	Concentration PDGFD (ng/ml)
809001	Melanoma	< 3
809002	Melanoma	< 3
809003	Melanoma	< 3
809004	Melanoma	< 3
809005	Melanoma	< 3
809006	Renal Cancer	< 3
809007	Renal Cancer	< 3
809008	Renal Cancer	< 3
809010	Renal Cancer	5.8
809010	Lung Cancer	< 3
809011	Lung Cancer	20
809012	Lung Cancer	10.04
809013	Myeloma	< 3
809014	Myeloma	< 3
809015	Myeloma	< 3
809016	Myeloma	< 3
809017	Myeloma	< 3
809018	Tongue Cancer	116.6
809019	Tongue Cancer	114.9
809020	Tongue Cancer	70.9
809021	Tongue Cancer	86.3
809022	Tongue Cancer	101.3
809023	Hodgkins	< 3
809024	Hodgkins	< 3
809025	Hodgkins	6.9
809026	Hodgkins	< 3
809027	Hodgkins	82.8
809028	Prostate Cancer	81.8
809029	Prostate Cancer	< 3
809030	Prostate Cancer	< 3

Sera number	Designation	Concentration PDGFD (ng/ml)
809031	Prostate Cancer	< 3
809032	Prostate Cancer	< 3
BRH00861	Cardiovascular	
BRH00862	Cardiovascular	
BRH00863	Cardiovascular	
BRH00864	Cardiovascular	
BRH00865	Cardiovascular	
817001	Scleroderma	
817002	Scleroderma	15.4
817003	Scleroderma	
817004	Scleroderma	
817005	Scleroderma	

EXAMPLE 4

It will be appreciated that based on the results set forth and discussed in Examples 2 and 3, through use of the present invention, it is possible to stage a cancer in a subject based on expression levels of the PDGFD antigen. For a given type of cancer, samples of blood are taken from subjects diagnosed as being at various stages in the progression of the disease, and/or at various points in the therapeutic treatment of the cancer. The concentration of the PDGFD antigen present in the blood samples is determined using a method that specifically determines the amount of the antigen that is present. Such a method includes an ELISA method, such as the method described in Examples 2 and 3. Using a population of samples that provides statistically significant results for each stage of progression or therapy, a range of concentrations of the antigen that may be considered characteristic of each stage is designated.

In order to stage the progression of the cancer in a subject under study, or to characterize the response of the subject to a course of therapy, a sample of blood is taken from the subject and the concentration of the PDGFD antigen present in the sample is determined. The concentration so obtained is used to identify in which range of concentrations the value falls. The range so identified correlates with a stage of progression or a stage of therapy identified in the various populations of diagnosed subjects, thereby providing a stage in the subject under study.

EXAMPLE 5

A sandwich ELISA was developed to quantify PDGF D levels in human serum. The 2 fully human mabs (1.6 and 1.17) used in the sandwich ELISA, recognized different epitopes on the PDGF D molecule (data not shown). The ELISA was performed as follows: 50 µl of capture antibody (mAb 1.6) in coating buffer (0.1 M $NaHCO_3$, pH 9.6) at a concentration of 2 µg/ml was coated on ELISA plates (Fisher). After incubation at 4°C overnight, the plates were treated with 200 µl of blocking buffer (0.5% BSA, 0.1% Tween 20, 0.01% Thimerosal in PBS) for 1 hr at 25°C. The plates were

washed (3x) using 0.05% Tween 20 in PBS (washing buffer, WB). Normal or patient sera (Clinomics, Bioreclaimation) were diluted in blocking buffer containing 50% human serum. The plates were incubated with serum samples overnight at 4°C, washed with WB, and then incubated with 100 µl/well of biotinylated detection antibody mAb 1.17 for 1 hr at 25°C. After washing, the plates were incubated with HRP-Streptavidin for 15 min, washed as before, and then treated with 100 µl/well of o-phenylenediamine in H_2O_2 (Sigma developing solution) for color generation. The reaction was stopped with 50 µl/well of H_2SO_4 (2M) and analyzed using an ELISA plate reader at 492 nm. Concentration of PDGF D in serum samples was calculated by comparison to dilutions of purified PDGF D using a four parameter curve fitting program.

EXAMPLE 6

PDGF D immunohistochemistry was performed with biotinylated fully human mAb 6.4 and streptavidin-HRP was used for detection. Briefly, tissues were deparaffinized using conventional techniques, and treated with trypsin (0.15%) for 10 min at 37 °C. Sections were incubated with 10% normal goat serum for 10 minutes. Normal goat serum solution was drained and wiped to remove excess solution. Sections were incubated with the biotinylated anti-PDGF D mAb at 5 µg/ml for 30 min at 25 °C, and washed thoroughly with PBS. After incubation with streptavidin-HRP conjugate for 10 min, a solution of diaminobenzidine (DAB) was applied onto the sections to visualize the immunoreactivity. For the isotype control, sections were incubated with biotinylated isotype matched negative control mAb at 5 µg/ml for 30 minutes at 25 °C instead of biotinylated PDGF D mAb.

EXAMPLE 7

In the following discussion, structural information related to antibodies prepared in accordance with the invention is provided.

In order to analyze structures of antibodies produced in accordance with the invention, we cloned genes encoding the heavy and light chain fragments out of the particular hybridoma. Gene cloning and sequencing was accomplished as follows:

Poly(A)$^+$ mRNA was isolated from approximately 2 X 10^5 hybridoma cells derived from immunized XenoMouse mice using a Fast-Track kit (Invitrogen). The generation of random primed cDNA was followed by PCR. Human V_H or human $V\kappa$ family specific variable region primers (Marks et. al., 1991) or a universal human V_H primer, MG-30 (CAGGTGCAGCTGGAGCAGTCIGG) (SEQ ID NO:51) was used in conjunction with primers specific for the human:

Cγ2 constant region (MG-40d; 5'-GCT GAG GGA GTA GAG TCC TGA GGA-3' (SEQ ID NO:52));

Cγ1 constant region (HG1; 5' CAC ACC GCG GTC ACA TGG C (SEQ ID NO:53)); or

Cγ3 constant region (HG3; 5' CTA CTC TAG GGC ACC TGT CC (SEQ ID NO:54))

or the human Cκ constant region (hκP2; as previously described in Green et al., 1994). Sequences of human Mabs-derived heavy and kappa chain transcripts from hybridomas were obtained by direct sequencing of PCR products generated from poly(A^+) RNA using the primers described above. PCR products were also cloned into pCRII using a TA cloning kit (Invitrogen) and both strands were sequenced using Prism dye-terminator sequencing kits and an ABI 377 sequencing machine. All sequences were analyzed by alignments to the "V BASE sequence directory" (Tomlinson et al., MRC Centre for Protein Engineering, Cambridge, UK) using MacVector and Geneworks software programs.

Figure 3 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.6 of the invention, with Figure 3A representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 3B representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 3A, Figure 3C representing the nucleotide sequence encoding the variable region of the light chain, and Figure 3D representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 3C.

Figure 4 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.11 of the invention, with Figure 4A representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 4B representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 4A, Figure 4C representing the nucleotide sequence encoding the variable region of the light chain, and Figure 4D representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 4C.

Figure 5 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.17 of the invention, with Figure 5A representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 5B representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 5A, Figure 5C representing the nucleotide sequence encoding the variable region of the light chain, and Figure 5D representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 5C.

Figure 6 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.18 of the invention, with Figure 6A representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 6B representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 6A, Figure 6C representing the nucleotide sequence encoding the variable region of the light chain, and Figure 6D representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 6C.

Figure 7 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.19 of the invention, with Figure 7A representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 7B representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 7A, Figure 7C representing the nucleotide sequence encoding the variable region of the light chain, and Figure 7D representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 7C.

Figure 8 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.23 of the invention, with Figure 8A representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 8B representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 8A, Figure 8C representing the nucleotide sequence encoding the variable region of the light chain, and Figure 8D representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 8C.

Figure 9 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.24 of the invention, with Figure 9A representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 9B representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 9A, Figure 9C representing the nucleotide sequence encoding the variable region of the light chain, and Figure 9D representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 9C.

Figure 10 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.25 of the invention, with Figure 10A representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 10B representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 10A, Figure 10C representing the nucleotide sequence encoding the variable region of the light chain, and Figure 10D representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 10C.

Figure 11 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.29 of the invention, with Figure 11A representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 11B representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 11A, Figure 11C representing the nucleotide sequence encoding the variable region of the light chain, and Figure 11D representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 11C.

Figure 12 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.33 of the invention, with Figure 12A representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 12B representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 12A, Figure 12C representing the nucleotide sequence encoding the variable region of the light chain, and Figure 12D representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 12C.

Figure 13 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.38 of the invention, with Figure 13A representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 13B representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 13A, Figure 13C representing the nucleotide sequence encoding the variable region of the light chain, and Figure 13D representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 13C.

Figure 14 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.39 of the invention, with Figure 14A representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 14B representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 14A, Figure 14C representing the nucleotide sequence encoding the variable region of the light chain, and Figure 14D representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 14C.

Figure 15 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.40 of the invention, with Figure 15A representing the nucleotide sequence encoding the variable region of the heavy chain and Figure 15B representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 15A.

Figure 16 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.45 of the invention, with Figure 16A representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 16B representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 16A, Figure 16C representing the nucleotide sequence encoding the variable region of the light chain, and Figure 16D representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 16C.

Figure 17 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.46 of the invention, with Figure 17A representing the nucleotide sequence

encoding the variable region of the heavy chain, Figure 17B representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 17A, Figure 17C representing the nucleotide sequence encoding the variable region of the light chain, and Figure 17D representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 17C.

Figure 18 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.48 of the invention, with Figure 18A representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 18B representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 18A, Figure 18C representing the nucleotide sequence encoding the variable region of the light chain, and Figure 18D representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 18C.

Figure 19 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.49 of the invention, with Figure 19A representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 19B representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 19A, Figure 19C representing the nucleotide sequence encoding the variable region of the light chain, and Figure 19D representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 19C.

Figure 20 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.51 of the invention, with Figure 20A representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 20B representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 20A, Figure 20C representing the nucleotide sequence encoding the variable region of the light chain, and Figure 20D representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 20C.

Figure 21 is a series of representations of the heavy chain and light chain variable region nucleotide and amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-6.4 of the invention, with Figure 21A representing the nucleotide sequence encoding the variable region of the heavy chain, Figure 21B representing the amino acid seqence encoded by the nucleotide sequence shown in Figure 21A, Figure 21C representing the nucleotide sequence encoding the variable region of the light chain, and Figure 21D representing the amino acid sequence encoded by the nucleotide sequence shown in Figure 21C.

Figure 22 is a table showing VDJ gene utilization of antibodies of the invention and indicating nucleotide/amino acid changes between the antibodies and the V, D, or J genes from which they are derived in the antibodies FR1, CDR1, FR2, CDR2, FR3, CDR3, and FR4 regions.

As will be observed in Figure 22A, the following antibodies have the following V heavy chain gene utilization:

VH 1-8: 1.19.1, 6.4.1, 1.18, 1.40.1, 1.45, 1.46.1, 1.49.1

VH 1-18: 1.33, 1.48.1

VH 3-21: 1.6.1

VH 3-33: 1.17.1, 1.24.1, 1.38.1

VH 3-53: 1.11.1

VH 5-51: 1.23.1, 1.25.1, 1.29, 1.39.1, 1.51.1

As will be observed in Figure 22B, the following antibodies have the following V light chain gene utilization:

VL L5: 1.48

VL A19: 1.49, 1.11, 1.29

VL A20: 1.45, 1.33, 1.38

VL A27: 6.4.1, 1.51

VL A30: 1.19, 1.18, 1.6, 1.23, 1.25, 1.29, 1.39, 1.17, 1.24, 1.46

For convenience, sequences of the protein sequences of the foregoing VH and VK genes are provided:

VH 1-8:
QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDINWVRQATGQGLEWMGWMNPNSGNTG
YAQKFQGRVTMTRNTSISTAYMELSSLRSEDTAVYYCARG (SEQ ID NO:1)

VH 1-18:
QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYGISWVRQAPGQGLEWMGWISAYNGNTNY
AQKLQGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCAR (SEQ ID NO:2)

VH 3-21:
EVQLVESGGGLVKPGGSLRLSCAASGFTFSSYSMNWVRQAPGKGLEWVSSISSSSSYIYYADS
VKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:3)

VH 3-33:
QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVIWYDGSNKYY
ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:4)

VH 3-53:
EVQLVESGGGLIQPGGSLRLSCAASGFTVSSNYMSWVRQAPGKGLEWVSVIYSGGSTYYADS
VKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:5)

VH 5-51:
EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGIIYPGDSDTRYSP
SFQGQVTISADKSISTAYLQWSSLKASDTAMYYCAR (SEQ ID NO:6)

VK L5:
DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIYAASSLQSGVPSRFS
GSGSGTDFTLTISSLQPEDFATYYCQQANSFP (SEQ ID NO:7)

VK A19:
DIVMTQSPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQLLIYLGSNRASGVP
DRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTP (SEQ ID NO:8)

VK A20:
DIQMTQSPSSLSASVGDRVTITCRASQGISNYLAWYQQKPGKVPKLLIYAASTLQSGVPSRFS
GSGSGTDFTLTISSLQPEDVATYYCQKYNSAP (SEQ ID NO:9)

VK A27:
EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFS
GSGSGTDFTLTISRLEPEDFAVYYCQQYGSSP (SEQ ID NO:10)

VK A30:
DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPGKAPKRLIYAASSLQSGVPSRFS
GSGSGTEFTLTISSLQPEDFATYYCLQHNSYP (SEQ ID NO:11)

Figure 23 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.6 of the invention and the V gene from which it is derived, with Figure 23A representing the alignment of the heavy chain amino acid sequence alignment and Figure 23B representing the alignment of the light chain amino acid sequence.

Figure 24 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.11 of the invention and the V gene from which it is derived, with Figure 24A representing the

alignment of the heavy chain amino acid sequence alignment and Figur 24B representing the alignment of the light chain amino acid sequence.

Figure 25 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.17 of the invention and the V gene from which it is derived, with Figure 25A representing the alignment of the heavy chain amino acid sequence alignment and Figure 25B representing the alignment of the light chain amino acid sequence.

Figure 26 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.18 of the invention and the V gene from which it is derived, with Figure 26A representing the alignment of the heavy chain amino acid sequence alignment and Figure 26B representing the alignment of the light chain amino acid sequence.

Figure 27 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.19 of the invention and the V gene from which it is derived, with Figure 27A representing the alignment of the heavy chain amino acid sequence alignment and Figure 27B representing the alignment of the light chain amino acid sequence.

Figure 28 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.23 of the invention and the V gene from which it is derived, with Figure 28A representing the alignment of the heavy chain amino acid sequence alignment and Figure 28B representing the alignment of the light chain amino acid sequence.

Figure 29 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.24 of the invention and the V gene from which it is derived, with Figure 29A representing the alignment of the heavy chain amino acid sequence alignment and Figure 29B representing the alignment of the light chain amino acid sequence.

Figure 30 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.25 of the invention and the V gene from which it is derived, with Figure 30A representing the alignment of the heavy chain amino acid sequence alignment and Figure 30B representing the alignment of the light chain amino acid sequence.

Figure 31 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.29 of the invention and the V gene from which it is derived, with Figure 31A representing the

alignment of the heavy chain amino acid sequence alignment and Figure 31B representing the alignment of the light chain amino acid sequence.

Figure 32 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.33 of the invention and the V gene from which it is derived, with Figure 32A representing the alignment of the heavy chain amino acid sequence alignment and Figure 32B representing the alignment of the light chain amino acid sequence.

Figure 33 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.38 of the invention and the V gene from which it is derived, with Figure 33A representing the alignment of the heavy chain amino acid sequence alignment and Figure 33B representing the alignment of the light chain amino acid sequence.

Figure 34 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.39 of the invention and the V gene from which it is derived, with Figure 34A representing the alignment of the heavy chain amino acid sequence alignment and Figure 34B representing the alignment of the light chain amino acid sequence.

Figure 35 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.45 of the invention and the V gene from which it is derived, with Figure 35A representing the alignment of the heavy chain amino acid sequence alignment and Figure 35B representing the alignment of the light chain amino acid sequence.

Figure 36 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.46 of the invention and the V gene from which it is derived, with Figure 36A representing the alignment of the heavy chain amino acid sequence alignment and Figure 36B representing the alignment of the light chain amino acid sequence.

Figure 37 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.48 of the invention and the V gene from which it is derived, with Figure 37A representing the alignment of the heavy chain amino acid sequence alignment and Figure 37B representing the alignment of the light chain amino acid sequence.

Figure 38 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.49 of the invention and the V gene from which it is derived, with Figure 38A representing the

alignment of the heavy chain amino acid sequence alignment and Figure 38B representing the alignment of the light chain amino acid sequence.

Figure 39 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-1.51 of the invention and the V gene from which it is derived, with Figure 39A representing the alignment of the heavy chain amino acid sequence alignment and Figure 39B representing the alignment of the light chain amino acid sequence.

Figure 40 is a series of alignments of the heavy chain and light chain variable region amino acid sequences of the human anti-PDGFD antibody expressed by the hybridoma cell line designated Cur 2-6.4 of the invention and the V gene from which it is derived, with Figure 40A representing the alignment of the heavy chain amino acid sequence alignment and Figure 40B representing the alignment of the light chain amino acid sequence.

Figure 41 is a table showing VDJ gene utilization of the 1.19.1 and 6.4.1 antibodies of the invention and indicating nucleotide changes between the antibodies and the VH, DH, and JH and VK and JK genes from which they are derived.

Figure 42 is a table showing VDJ gene utilization of the 1.6.1, 1.11.1, and 1.23.1 antibodies of the invention and indicating nucleotide changes between the antibodies and the VH, DH, and JH and VK and JK genes from which they are derived.

Figure 43 is a table showing VDJ gene utilization of the 1.19.1, 6.4.1, 1.6.1, 1.11.1, 1.23.1, 1.17.1, 1.18, 1.24.1, 1.25.1, 1.29, 1.33, 1.38.1, 1.39.1, 1.40.1, 1.45, 1.46.1, 1.46.2, 1.48.1, 1.49.1, and 1.51.1 antibodies of the invention and indicating nucleotide changes between the antibodies and the VH, DH, and JH and VK and JK genes from which they are derived.

Figure 48 is a representation of a ClustalW sequence alignment between the heavy chain amino acid sequences of antibodies of the invention indicating locations of the CDRs of the antibodies.

Figure 49 is a representation of a ClustalW sequence alignment between the light chain amino acid sequences of antibodies of the invention indicating locations of the CDRs of the antibodies.

Figure 50 is a representation of a ClustalW sequence alignment between the heavy chain amino acid sequences of antibodies of the invention that possess heavy chains derived from the VH 1-8 gene with CDRs indicated.

Figure 51 is a representation of a ClustalW sequence alignment between the heavy chain amino acid sequences of antibodies of the invention that possess heavy chains derived from the VH 1-18 gene with CDRs indicated.

Figure 52 is a representation of a ClustalW sequence alignment between the heavy chain amino acid sequences of antibodies of the invention that possess heavy chains derived from the VH 3-33 gene with CDRs indicated.

Figure 53 is a representation of a ClustalW sequence alignment between the heavy chain amino acid sequences of antibodies of the invention that possess heavy chains derived from the VH 5-51 gene with CDRs indicated.

Figure 54 is a representation of a ClustalW sequence alignment between the light chain amino acid sequences of antibodies of the invention that possess light chains derived from the VK A19 gene with CDRs indicated.

Figure 55 is a representation of a ClustalW sequence alignment between the light chain amino acid sequences of antibodies of the invention that possess light chains derived from the VK A20 gene with CDRs indicated.

Figure 56 is a representation of a ClustalW sequence alignment between the light chain amino acid sequences of antibodies of the invention that possess light chains derived from the VK A27 gene with CDRs indicated.

Figure 57 is a representation of a ClustalW sequence alignment between the light chain amino acid sequences of antibodies of the invention that possess light chains derived from the VK A30 gene with CDRs indicated.

In each of Figures 48-57, CDR domains were determined in accordance with the Kabat numbering system. *See* Kabat *Sequences of Proteins of Immunological Interest* (National Institutes of Health, Bethesda, Md. (1987 and 1991)).

EXAMPLE 8

In the following discussion, structural information related to relative epitopes that antibodies prepared in accordance with the invention bind to is provided.

Certain antibodies in accordance with the present invention were "binned" in accordance relative epitope to which they bind. In order to conduct such binning, we followed the protocol described in U.S. Patent Application No. 60/337,245, filed December 3, 2001, entitled Antibody Categorization Based On Binding Characteristics. As shown in the following Tables, we detected antibodies that bound to at least three distinct epitopes on the PDGFD antigen. Results are shown for two different experiments utilizing the binning procedure described in the foregoing patent application as well as results derived from competition studies using BiaCore affinity cross-competition studies.

Epitope Type			
I	II	III	IV
1.6	1.9	1.45	1.33
1.19	1.22	1.46	
	1.29		
	6.4		
Epitope Type			
I	II	III	IV
1.6	1.9	1.19	1.33
	1.29	1.22	
	1.45	6.4	
	1.46		
Epitope Type (by BiaCore)			
I	II	IV	?
1.6	1.9	6.4	1.33
1.45	1.19		1.46
	1.22		
	1.29		

EQUIVALENTS

The foregoing description and Examples detail certain preferred embodiments of the invention and describes the best mode contemplated by the inventors. It will be appreciated, however, that no matter how detailed the foregoing may appear in text, the invention may be practiced in many ways and the invention should be construed in accordance with the appended claims and any equivalents thereof.

WHAT WE CLAIM IS:

1. A human monoclonal antibody that binds to PDGFD and comprises a heavy chain amino acid sequence selected from the group consisting of SEQ ID NOS: 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 38, 40, 42, 44, 46, and 48.

2. The antibody of Claim 1, further comprising a light chain amino acid sequence selected from the group consisting of SEQ ID NOS:14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 39, 41, 43, 45, 47, and 49.

3. The human monoclonal antibody of claim 2, wherein the heavy chain amino sequence comprises the sequence of SED ID NO:13 and the light chain amino acid comprises the sequence of SEQ ID NO:14.

4. The human monoclonal antibody of claim 2, wherein the heavy chain amino sequence comprises the sequence of SED ID NO:15 and the light chain amino acid comprises the sequence of SEQ ID NO:16.

5. The human monoclonal antibody of claim 2, wherein the heavy chain amino sequence comprises the sequence of SED ID NO:17 and the light chain amino acid comprises the sequence of SEQ ID NO:18.

6. The human monoclonal antibody of claim 2, wherein the heavy chain amino sequence comprises the sequence of SED ID NO:19 and the light chain amino acid comprises the sequence of SEQ ID NO:20.

7. The human monoclonal antibody of claim 2, wherein the heavy chain amino sequence comprises the sequence of SED ID NO:21 and the light chain amino acid comprises the sequence of SEQ ID NO:22.

8. The human monoclonal antibody of claim 2, wherein the heavy chain amino sequence comprises the sequence of SED ID NO:23 and the light chain amino acid comprises the sequence of SEQ ID NO:24.

9. The human monoclonal antibody of claim 2, wherein the heavy chain amino sequence comprises the sequence of SED ID NO:25 and the light chain amino acid comprises the sequence of SEQ ID NO:26.

10. The human monoclonal antibody of claim 2, wherein the heavy chain amino sequence comprises the sequence of SED ID NO:27 and the light chain amino acid comprises the sequence of SEQ ID NO:28.

11. The human monoclonal antibody of claim 2, wherein the heavy chain amino sequence comprises the sequence of SED ID NO:29 and the light chain amino acid comprises the sequence of SEQ ID NO:30.

12. The human monoclonal antibody of claim 2, wherein the heavy chain amino sequence comprises the sequence of SED ID NO:31 and the light chain amino acid comprises the sequence of SEQ ID NO:32.

13. The human monoclonal antibody of claim 2, wherein the heavy chain amino sequence comprises the sequence of SED ID NO:33 and the light chain amino acid comprises the sequence of SEQ ID NO:34.

14. The human monoclonal antibody of claim 2, wherein the heavy chain amino sequence comprises the sequence of SED ID NO:35 and the light chain amino acid comprises the sequence of SEQ ID NO:36.

15. The human monoclonal antibody of claim 2, wherein the heavy chain amino sequence comprises the sequence of SED ID NO:37.

16. The human monoclonal antibody of claim 2, wherein the heavy chain amino sequence comprises the sequence of SED ID NO:38 and the light chain amino acid comprises the sequence of SEQ ID NO:39.

17. The human monoclonal antibody of claim 2, wherein the heavy chain amino sequence comprises the sequence of SED ID NO:40 and the light chain amino acid comprises the sequence of SEQ ID NO:41.

18. The human monoclonal antibody of claim 2, wherein the heavy chain amino sequence comprises the sequence of SED ID NO:42 and the light chain amino acid comprises the sequence of SEQ ID NO:43.

19. The human monoclonal antibody of claim 2, wherein the heavy chain amino sequence comprises the sequence of SED ID NO:44 and the light chain amino acid comprises the sequence of SEQ ID NO:45.

20. The human monoclonal antibody of claim 2, wherein the heavy chain amino sequence comprises the sequence of SED ID NO:46 and the light chain amino acid comprises the sequence of SEQ ID NO:47.

21. The human monoclonal antibody of claim 2, wherein the heavy chain amino sequence comprises the sequence of SED ID NO:48 and the light chain amino acid comprises the sequence of SEQ ID NO:49.

CTAAAAAATATGTTCTCTACAACACCAAGGCTCATTAAAATATTTTAAATATTAATATACAT
TTCTTCTGTCAGAAATACATAAAACTTTATTATATCAGCGCAGGGCGGCGCGGCGTCGGTCC
CGGGAGCAGAACCCGGCTTTTTCTTGGAGCGACGCTGTCTCTAGTCGCTGATCCCAAATGCA
CCGGCTCATCTTTGTCTACACTCTAATCTGCGCAAACTTTTGCAGCTGTCGGGACACTTCTG
CAACCCCGCAGAGCGCATCCATCAAAGCTTTGCGCAACGCCAACCTCAGGCGAGATGAGAGC
AATCACCTCACAGACTTGTACCGAAGAGATGAGACCATCCAGGTGAAAGGAAACGGCTACGT
GCAGAGTCCTAGATTCCCGAACAGCTACCCCAGGAACCTGCTCCTGACATGGCGGCTTCACT
CTCAGGAGAATACACGGATACAGCTAGTGTTTGACAATCAGTTTGGATTAGAGGAAGCAGAA
AATGATATCTGTAGGTATGATTTTGTGGAAGTTGAAGATATATCCGAAACCAGTACCATTAT
TAGAGGACGATGGTGTGGACACAAGGAAGTTCCTCCAAGGATAAAATCAAGAACGAACCAAA
TTAAAATCACATTCAAGTCCGATGACTACTTTGTGGCTAAACCTGGATTCAAGATTTATTAT
TCTTTGCTGGAAGATTTCCAACCCGCAGCAGCTTCAGAGACCAACTGGGAATCTGTCACAAG
CTCTATTTCAGGGGTATCCTATAACTCTCCATCAGTAACGGATCCCACTCTGATTGCGGATG
CTCTGGACAAAAAAATTGCAGAATTTGATACAGTGGAAGATCTGCTCAAGTACTTCAATCCA
GAGTCATGGCAAGAAGATCTTGAGAATATGTATCTGGACACCCCTCGGTATCGAGGCAGGTC
ATACCATGACCGGAAGTCAAAAGTTGACCTGGATAGGCTCAATGATGATGCCAAGCGTTACA
GTTGCACTCCCAGGAATTACTCGGTCAATATAAGAGAAGAGCTGAAGTTGGCCAATGTGGTC
TTCTTTCCACGTTGCCTCCTCGTGCAGCGCTGTGGAGGAAATTGTGGCTGTGGAACTGTCAA
CTGGAGGTCCTGCACATGCAATTCAGGGAAAACCGTGAAAAAGTATCATGAGGTATTACAGT
TTGAGCCTGGCCACATCAAGAGGAGGGGTAGAGCTAAGACCATGGCTCTAGTTGACATCCAG
TTGGATCACCATGAACGATGTGATTGTATCTGCAGCTCAAGACCACCTCGATAAGAGAATGT
GCACATCCTTACATTAAGCCTGAAAGAACCTTTAGTTTAAGGAGGGTGAGATAAGAGACCCT
TTTCCTACCAGCAACCAAACTTACTACTAGCCTGCAATGCAATGAACACAAGTGGTTGCTGA
GTCTCAGCCTTGCTTTGTTAATGCCATGGCAAGTAGAAAGGTATATCATCAACTTCTATACC
TAAGAATATAGGATTGCATTTAATAATAGTGTTTGAGGTTATATATGCACAAACACACACAG
AAATATATTCATGTCTATGTGTATATAGATCAAATGTTTTTTTTGGTATATATAACCAGGTA
CACCAGAGCTTACATATGTTTGAGTTAGACTCTTAAAATCCTTTGCCAAAATAAGGGATGGT
CAAATATATGAAACATGTCTTTAGAAAATTTAGGAGATAAATTTATTTTTAAATTTTGAAAC
ACAAAACAATTTTGAATCTTGCTCTCTTAAAGAAAGCATCTTGTATATTAAAAATCAAAAGA
TGAGGCTTTCTTACATATACATCTTAGTTG (SEQ ID NO:50)

FIG. 1

```
  1 CTAAAAAATATGTTCTCTACAACACCAAGGCTCATTAAAATATTT
 46 TAAATATTAATATACATTTCTTCTGTCAGAAATACATAAAACTTT
 91 ATTATATCAGCGCAGGGCGGCGCGGCGTCGGTCCCGGGAGCAGAA
136 CCCGGCTTTTTCTTGGAGCGACGCTGTCTCTAGTCGCTGATCCCA

181 AATGCACCGGCTCATCTTTGTCTACACTCTAATCTGCGCAAACTT
     MetHisArgLeuIlePheValTyrThrLeuIleCysAlaAsnPhe

226 TTGCAGCTGTCGGGACACTTCTGCAACCCCGCAGAGCGCATCCAT
    CysSerCysArgAspThrSerAlaThrProGlnSerAlaSerIle

271 CAAAGCTTTGCGCAACGCCAACCTCAGGCGAGATGAGAGCAATCA
    LysAlaLeuArgAsnAlaAsnLeuArgArgAspGluSerAsnHis

316 CCTCACAGACTTGTACCGAAGAGATGAGACCATCCAGGTGAAAGG
    LeuThrAspLeuTyrArgArgAspGluThrIleGlnValLysGly

361 AAACGGCTACGTGCAGAGTCCTAGATTCCCGAACAGCTACCCCAG
    AsnGlyTyrValGlnSerProArgPheProAsnSerTyrProArg

406 GAACCTGCTCCTGACATGGCGGCTTCACTCTCAGGAGAATACACG
    AsnLeuLeuLeuThrTrpArgLeuHisSerGlnGluAsnThrArg

451 GATACAGCTAGTGTTTGACAATCAGTTTGGATTAGAGGAAGCAGA
    IleGlnLeuValPheAspAsnGlnPheGlyLeuGluGluAlaGlu

496 AAATGATATCTGTAGGTATGATTTTGTGGAAGTTGAAGATATATC
    AsnAspIleCysArgTyrAspPheValGluValGluAspIleSer

541 CGAAACCAGTACCATTATTAGAGGACGATGGTGTGGACACAAGGA
    GluThrSerThrIleIleArgGlyArgTrpCysGlyHisLysGlu

586 AGTTCCTCCAAGGATAAAATCAAGAACGAACCAAATTAAAATCAC
    ValProProArgIleLysSerArgThrAsnGlnIleLysIleThr
```

FIG. 2A

631 ATTCAAGTCCGATGACTACTTTGTGGCTAAACCTGGATTCAAGAT
PheLysSerAspAspTyrPheValAlaLysProGlyPheLysIle

676 TTATTATTCTTTGCTGGAAGATTTCCAACCCGCAGCAGCTTCAGA
TyrTyrSerLeuLeuGluAspPheGlnProAlaAlaAlaSerGlu

721 GACCAACTGGGAATCTGTCACAAGCTCTATTTCAGGGGTATCCTA
ThrAsnTrpGluSerValThrSerSerIleSerGlyValSerTyr

766 TAACTCTCCATCAGTAACGGATCCCACTCTGATTGCGGATGCTCT
AsnSerProSerValThrAspProThrLeuIleAlaAspAlaLeu

811 GGACAAAAAAATTGCAGAATTTGATACAGTGGAAGATCTGCTCAA
AspLysLysIleAlaGluPheAspThrValGluAspLeuLeuLys

856 GTACTTCAATCCAGAGTCATGGCAAGAAGATCTTGAGAATATGTA
TyrPheAsnProGluSerTrpGlnGluAspLeuGluAsnMetTyr

901 TCTGGACACCCCTCGGTATCGAGGCAGGTCATACCATGACCGGAA
LeuAspThrProArgTyrArgGlyArgSerTyrHisAspArgLys

946 GTCAAAAGTTGACCTGGATAGGCTCAATGATGATGCCAAGCGTTA
SerLysValAspLeuAspArgLeuAsnAspAspAlaLysArgTyr

991 CAGTTGCACTCCCAGGAATTACTCGGTCAATATAAGAGAAGAGCT
SerCysThrProArgAsnTyrSerValAsnIleArgGluGluLeu

1036 GAAGTTGGCCAATGTGGTCTTCTTTCCACGTTGCCTCCTCGTGCA
LysLeuAlaAsnValValPhePheProArgCysLeuLeuValGln

1081 GCGCTGTGGAGGAAATTGTGGCTGTGGAACTGTCAACTGGAGGTC
ArgCysGlyGlyAsnCysGlyCysGlyThrValAsnTrpArgSer

1126 CTGCACATGCAATTCAGGGAAAACCGTGAAAAAGTATCATGAGGT
CysThrCysAsnSerGlyLysThrValLysLysTyrHisGluVal

1171 ATTACAGTTTGAGCCTGGCCACATCAAGAGGAGGGGTAGAGCTAA
LeuGlnPheGluProGlyHisIleLysArgArgGlyArgAlaLys

FIG. 2B

```
1216 GACCATGGCTCTAGTTGACATCCAGTTGGATCACCATGAACGATG
     ThrMetAlaLeuValAspIleGlnLeuAspHisHisGluArgCys

1261 TGATTGTATCTGCAGCTCAAGACCACCTCGATAAGAGAATGTGCA
     AspCysIleCysSerSerArgProProArg (SEQ ID NO:12)

1306 CATCCTTACATTAAGCCTGAAAGAACCTTTAGTTTAAGGAGGGTG
1351 AGATAAGAGACCCTTTTCCTACCAGCAACCAAACTTACTACTAGC
1396 CTGCAATGCAATGAACACAAGTGGTTGCTGAGTCTCAGCCTTGCT
1441 TTGTTAATGCCATGGCAAGTAGAAAGGTATATCATCAACTTCTAT
1486 ACCTAAGAATATAGGATTGCATTTAATAATAGTGTTTGAGGTTAT
1531 ATATGCACAAACACACACAGAAATATATTCATGTCTATGTGTATA
1576 TAGATCAAATGTTTTTTTTGGTATATATAACCAGGTACACCAGAG
1621 CTTACATATGTTTGAGTTAGACTCTTAAAATCCTTTGCCAAAATA
1666 AGGGATGGTCAAATATATGAAACATGTCTTTAGAAAATTTAGGAG
1711 ATAAATTTATTTTTAAATTTTGAAACACAAAACAATTTTGAATCT
1756 TGCTCTCTTAAAGAAAGCATCTTGTATATTAAAAATCAAAAGATG
1801 AGGCTTTCTTACATATACATCTTAGTTG (SEQ ID NO:50)
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FIG. 2C

A -- Cur2 1.6 heavy chain nucleotide sequence

GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCCTGGTCAAGCCTGGGGGGTCCCTGAGACTCTC
CTGTGCAGCCTCTGGATTCAACTTCAGAACCTATAACATGAACTGGGTCCGCCAGGCTCCAG
GGAAGGGGCTGGAGTGGGTCTCATCCATTAGTAGTAGTAGTAGTAACATATACTACGCAGAC
TCAGTGAAGGGCCGATTCACCATCTCCAGAGACAACGCCAAGAACTCACTGTATCTGCAAAT
GAACAGCCTGAGAGCCGAGGACACGGCTGTATATTACTGTGCGAGAGATATTATGATTACGT
TTGGGGGAATTATCGCCTCGTTCTACTTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTC
TCCTCAG (SEQ ID NO:55)

B -- Cur2 1.6 heavy chain amio acid sequence

EVQLVESGGGLVKPGGSLRLSCAASGFNFRTYNMNWVRQAPGKGLEWVSSISSSSSNIYYAD
SVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDIMITFGGIIASFYFDYWGQGTLVTV
SS (SEQ ID NO:13)

C -- Cur2 1.6 light chain nucleotide sequence

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT
CACTTGCCGGGCAAGTCAGGGCATTAGAAATGATTTAGGCTGGTTTCAGCAGAAACCAGGGA
AAGCCCCTAAGCGCCTGATCTATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTC
AGCGGCAGTGGATCTGGGACAGAATTCACTCTCACAATCAGCAGCCTGCAGCCTGAAGATTT
TGCAACTTATTACTGTCTACAGCATAATAGTTACCCGCTCACTTTCGGCGGAGGGACCAAGG
TGGAGATCAAAC (SEQ ID NO:56)

D -- Cur2 1.6 light chain amino acid sequence

DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWFQQKPGKAPKRLIYAASSLQSGVPSRF
SGSGSGTEFTLTISSLQPEDFATYYCLQHNSYPLTFGGGTKVEIK (SEQ ID NO:14)

FIG. 3

A -- Cur2 1.11 heavy chain nucleotide sequence

GAGGTGCAGCTGGTGCAGTCTGGAGGAGGCTTGATCCAGCCTGGGGGGTCCCTGAGACTCTC
CTGTGCAGCCTCTGGGTTCACCGTCAGTAGCAACTACATGAGCTGGGTCCGCCAGGCTCCAG
GGAAGGGGCTGGAGTGGGTCTCAGTTATTTATAGCGGTGGTAGCACATACTACGCAGACTCC
GTGAAGGGCCGATTCACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTTCAAATGAA
CAGCCTGAGAGCCGAGGACACGGCCGTGTATTACTGTGCGGGAACGGTGACTACGAATTACT
ACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCCTCAG
(SEQ ID NO:57)

B -- Cur2 1.11 heavy chain amino acid sequence

EVQLVQSGGGLIQPGGSLRLSCAASGFTVSSNYMSWVRQAPGKGLEWVSVIYSGGSTYYADS
VKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAGTVTTNYYYGMDVWGQGTTVTVSS
(SEQ ID NO:15)

C -- Cur2 1.11 light chain nucleotide sequence

GATATTGTGATGACTCAGTCTCCACTCTCCCTGCCCGTCACCCCTGGAGAGCCGGCCTCCAT
CTCCTGCAGGTCTAGTCAGAGCCTCCTGCAAAGTAATGGATACAACTATTTGGATTGGTACC
TGCAGAAGCCAGGGCAGTCTCCACAGCTCCTGATCTATTTGGGTTCTAATCGGGCCTCCGGG
GTCCCTGACAGGTTCAGTGGCAGTGGATCAGGCACAGATTTTACACTGAAAATCAGCAGAGT
GGAGGCTGAGGATGTTGGGGTTTATTACTGCATGCAAGCTCTACAAACTCTCACTTTCGGCG
GAGGGACCAAGGTGGAGATCAAAC (SEQ ID NO:58)

D -- Cur2 1.11 light chain amino acid sequence

DIVMTQSPLSLPVTPGEPASISCRSSQSLLQSNGYNYLDWYLQKPGQSPQLLIYLGSNRASG
VPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTLTFGGGTKVEIK
(SEQ ID NO:16)

FIG. 4

A -- Cur2 1.17 heavy chain nucleotide sequence

CAGGTGCAGCTGGTGGAGTCGGGGGGAGGCGTGGTCCAGCCTGGGAAGTCCCTGAGACTCTC
CTGTGCAGCGTCTGGATTCACCTTCAGTAGCTATGGCATGCACTGGGTCCGCCAGGCTCCAG
GCAAGGGGCTGGAGTGGGTGGCAGTTATATGGTATGATGGAAGTAATAAATACTATGCAGAC
TCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTGCAAAT
GAACAGCCTGAGAGCCGAGGACACGGCTGTGTATTACTGTGCGAGAGATCAAGGATACAGAT
ATGCTGGTTACTACTACGACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTC
TCCTCAG (SEQ ID NO:59)

B -- Cur2 1.17 heavy chain protein sequence

QVQLVESGGGVVQPGKSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVIWYDGSNKYYAD
SVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDQGYRYAGYYYDYGMDVWGQGTTVTV
SS (SEQ ID NO:17)

C -- Cur2 1.17 light chain nucleotide sequence

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT
CACTTGCCGGGCAAGTCAGGGCATTAGAAATGATTTAGGCTGGTATCAGCAGAAACCAGGGA
AAGCCCCTAAGCGCCTGATCTATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTC
AGCGGCAGTGGATCTGGGACAGAATTCACTCTCACAATCAGCAGCCTGCAGCCTGAAGATTT
TGCAACTTATTACTGTCTACAGCATAATAGTTACCCGCTCACTTTCGGCGGAGGGACCAAGG
TGGAGATCAAAC (SEQ ID NO:60)

D -- Cur2 1.17 light chain protein sequence

DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPGKAPKRLIYAASSLQSGVPSRF
SGSGSGTEFTLTISSLQPEDFATYYCLQHNSYPLTFGGGTKVEIK (SEQ ID NO:18)

FIG. 5

A -- Cur2 1.18 heavy chain nucleotide sequence

CAGGTGCAGCTGGTGCAGTCGGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGTGAAGGTCTC
CTGCAAGGCTTCTGGATACACCTTCACCAGTTATGATATCAACTGGGTGCGACAGGCCACTG
GACAAGGGCTTGAGTGGATGGGATGGATGAACCCAAACAGTGGTAACACAGGCTATGCACAG
AAGTTCCAGGGCAGAGTCACCATGACCAGGAACACCTCCATAAGCACAGCCTACATGGAGCT
GAGCAGCCTGAGATCTGAGGACACGGCCGTGTATTACTGTGCGAGAGAGGGTATAGCAGTGG
CTGGGACATACTACTACTACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTC
TCCTCAG (SEQ ID NO:61)

B -- Cur2 1.18 heavy chain protein sequence

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDINWVRQATGQGLEWMGWMNPNSGNTGYAQ
KFQGRVTMTRNTSISTAYMELSSLRSEDTAVYYCAREGIAVAGTYYYYYGMDVWGQGTTVTV
SS (SEQ D NO:19)

C -- Cur2 1.18 light chain nucleotide sequence

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT
CACTTGCCGGGCAAGTCAGGGCATTAGAAATGATTTAGGCTGGTATCAGCAGAAACCAGGGA
AAGCCCCTAAGCGCCTGATCTATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTC
AGCGGCAGTGGATCTGGGACAGAATTCACTCTCACAATCAGCAGCCTGCAGCCTGAAGATTT
TGCAACTTATTTCTGTCTACAGCATAATAGTTACCCATTCACTTTCGGCCCTGGGACCAAAG
TGGATATCAAAC (SEQ ID NO:62)

D -- Cur2 1.18 light chain protein sequence

DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPGKAPKRLIYAASSLQSGVPSRF
SGSGSGTEFTLTISSLQPEDFATYFCLQHNSYPFTFGPGTKVDIK (SEQ ID NO:20)

FIG. 6

A -- Cur2 1.19 heavy chain nucleotide sequence

CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGTGAAGGTCTC
CTGCAAGGCTTCTGGATACACCTTCACCAGTTATGATATCAACTGGGTGCGACAGGCCACTG
GACAAGGGCTTGAGTGGATGGGATGGATGAACCCTAACAGTGGTAACACAGGCTATGCACAG
AAGTTCCAGGGCAGAGTCACCATGACCAGGAACACCTCCATAAGCACAGCCTACATGGAGCT
GAGCAGCCTGAGATCTGAGGACACGGCCGTGTATTACTGTGCGAGAGACGTTATGATTACGT
TTGGGGGAGTTATCGTGCACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTC
TCCTCAG (SEQ ID NO:63)

B -- Cur2 1.19 heavy chain amino acid sequence

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDINWVRQATGQGLEWMGWMNPNSGNTGYAQ
KFQGRVTMTRNTSISTAYMELSSLRSEDTAVYYCARDVMITFGGVIVHYGMDVWGQGTTVTV
SS (SEQ ID NO:21)

C -- Cur2 1.19 light chain nucleotide sequence

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT
CACTTGCCGGGCAAGTCAGGGCATTAGAAATGATTTAGGCTGGTATCAGCAGAAACCAGGGA
AAGCCCCTAAGCGCCTGATCTATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTC
AGCGGCAGTGGATCTGGGACAGATTTCACTCTCACAATCAGCAGCCTGCAGCCTGAAGATTT
TGCAACTTATTACTGTCTACAGCATAATAGTGACCCGTGCAGTTTTGGCCAGGGGACCAAGC
TGGAGATCAGAC (SEQ ID NO:64)

D -- Cur2 1.19 light chain amino acid sequence

DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPGKAPKRLIYAASSLQSGVPSRF
SGSGSGTDFTLTISSLQPEDFATYYCLQHNSDPCSFGQGTKLEIR (SEQ ID NO:22)

FIG. 7

A -- Cur2 1.23 heavy chain nucleotide sequence

GAGGTGCAGCTGGTGCAGTCTGGAGCAGAGGTGAAAAAGCCCGGGGAGTCTCTGAAGATCTC
CTGTGAGGGTTCTGGATACAGCTTTACCAGCTACTGGATCGGCTGGGTGCGCCAGATGCCCG
GGAAAGGCCTGGAGTGGATGGGGATCATCTATCCTGGTGACTCTGATACCAGATACAGCCCG
TCCTTCCAAGGCCAGGTCACCATCTCAGCCGACAAGTCCATCAGCACCGCCTACCTGCAGTG
GAGCAGCCTGAAGGCCTCGGACACCGCCATGTATTACTGTGCGAGACATGTATCGTATTACT
ATGTTTCGGGGAGTTATTATAACGTCTTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTC
TCCTCAG (SEQ ID NO:65)

B -- Cur2 1.23 heavy chain amino acid sequence

EVQLVQSGAEVKKPGESLKISCEGSGYSFTSYWIGWVRQMPGKGLEWMGIIYPGDSDTRYSP
SFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARHVSYYYVSGSYYNVFDYWGQGTLVTV
SS (SEQ ID NO:23)

C -- Cur2 1.23 light chain nucleotide sequence

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT
CACTTGCCGGGCAAGTCAGGGCATTAGAAATGATTTAGGCTGGTATCAGCAGATACCAGGGA
AAGCCCCTAAGCGCCTGATCTATGCTGCATCCAGTTTGCAACGTGGGGTCCCATCAAGGTTC
AGCGGCAGTGGATCTGGGACAGAATTCACTCTCACAATCAGCAGCCTGCAGCCTGAAGATTT
TGCAACTTATTACTGTCTACAGCATAATAGTTACCCGTGGACGTTCGGCCAAGGGACCAAGG
TGGAAATCAAAC (SEQ ID NO:66)

D -- Cur2 1.23 light chain amino acid sequence

DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQIPGKAPKRLIYAASSLQRGVPSRF
SGSGSGTEFTLTISSLQPEDFATYYCLQHNSYPWTFGQGTKVEIK (SEQ ID NO:24)

FIG. 8

A -- Cur2 1.24.1 heavy chain nucleotide sequence

CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTC
CTGTGCAGCGTCTGGATTCAGTTTCAGTAGCTATGGCATGCACTGGGTCCGCCAGGCTCCAG
GCAAGGGGCTGGAGTGGGTGGCAGATATATGGTATGATGGAAGTAATAAATACTATGCAGAC
TCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTGCAAAT
GAACAGCCTGAGAGCCGAGGACACGGCTGTGTATTATTGTGCGAGAGATCAGGGATACAGCT
ATGGTTACGTCTACTACGACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTC
TCCTCAG (SEQ ID NO:67)

B -- Cur2 1.24.1 heavy chain protein sequence

QVQLVESGGGVVQPGRSLRLSCAASGFSFSSYGMHWVRQAPGKGLEWVADIWYDGSNKYYAD
SVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDQGYSYGYVYYDYGMDVWGQGTTVTV
SS (SEQ ID NO:25)

C -- Cur2 1.24.1 light chain nucleotide sequence

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT
CACTTGCCGGGCAAGTCAGGGCATTAGAAATGATTTAGGCTGGTATCAGCAGAAACCAGGGA
AAGCCCCTAAGCGCCTGATCTATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTC
AGCGGCAGTGGATCTGGGACAGAGTTCACTCTCACAATCAGCAGCCTGCAGCCTGAAGATTT
TGCAACTTATTACTGTCTACAGCATAATAGTTACCCGTGGACGTTCGGCCAAGGGACCAAGG
TGGAAATCAAAC (SEQ ID NO:68)

D -- Cur2 1.24.1 light chain protein sequence

DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPGKAPKRLIYAASSLQSGVPSRF
SGSGSGTEFTLTISSLQPEDFATYYCLQHNSYPWTFGQGTKVEIK (SEQ ID NO:26)

FIG. 9

A -- Cur2 1.25.1 heavy chain nucleotide sequence

GAGGTGCAGCTGGTGCAGTCGGGAGCAGAGGTGAAAAAGCCCGGGGAGTCTCTGAAGATCTC
CTGTAAGGGTTCTGGATACAGGTTTACCAGCTACTGGATCGGCTGGGTGCGCCAGATGCCCG
GGAAAGGCCTGGAGTGGATGGGGATCATCTATCCTGGTGACTCTGATACCAGATACAGCCCG
TCCTTCCAAGGCCAGGTCACCATCTCAGCCGACAAGTCCATCAGCACCGCCTACCTGCAGTG
GAGCAGCCTGAAGGCCTCGGACACCGCCATGTATTACTGTGCGAGACATGGATCGTATTATT
ATGGTTCGGAGACTTATTATAATGTCTTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTC
TCCTCAG (SEQ ID NO:69)

B -- Cur2 1.25.1 heavy chain protein sequence

EVQLVQSGAEVKKPGESLKISCKGSGYRFTSYWIGWVRQMPGKGLEWMGIIYPGDSDTRYSP
SFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARHGSYYYGSETYYNVFDYWGQGTLVTV
SS (SEQ ID NO:27)

C -- Cur2 1.25.1 light chain nucleotide sequence

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT
CACTTGCCGGGCAAGTCAGGGCATTAGAAATGATTTAGGCTGGTATCAGCAGAAACCAGGGA
AAGCCCCTAAGCGCCTGATCTATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTC
AGCGGCAGTGGATCTGGGACAGAATTCACTCTCACAATCAGCAGCCTGCAGCCTGAAGATTT
TGCAACTTATTACTGTCTACAGCATAATAGTTACCCGTGGACGTTCGGCCAAGGGACCAAGG
TGGAAATCAAAC (SEQ ID NO:70)

D -- Cur2 1.25.1 light chain protein sequence

DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPGKAPKRLIYAASSLQSGVPSRF
SGSGSGTEFTLTISSLQPEDFATYYCLQHNSYPWTFGQGTKVEIK (SEQ ID NO:28)

FIG. 10

A -- Cur2 1.29 heavy chain nucleotide sequence

GAGGTGCAGCTGGTGCAGTCGGGAGCAGAGGTGAAAAAGCCCGGGGAGTCTCTGAAGATCTC
CTGTAAGGGTTCTGGATACAGCTTTACCAGCTACTGGATCGGCTGGGTGCGCCAGATGCCCG
GGAAAGGCCTGGAGTGGATGGGGATCATCTATCCTGGTGACTCTGATACCAGATACAGCCCG
TCCTTCCAAGGCCAGGCCACCATCTCAGCCGACAAGTCCATCAGCACCGCCTACCTGCAGTG
GAGCAGCCTGAAGGCCTCGGACACCGCCATGTATTACTGTGCGAGACACGTGGATGTAGGGG
CTACGATTGGGGGATATTACTATTACTACCACGGTATGGACGTCTGGGGCCAAGGGACCACG
GTCACCGTCTCCTCAG (SEQ ID NO:71)

B -- Cur2 1.29 heavy chain protein sequence

EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGIIYPGDSDTRYSP
SFQGQATISADKSISTAYLQWSSLKASDTAMYYCARHVDVGATIGGYYYYYHGMDVWGQGTT
VTVSS (SEQ ID NO:29)

C -- Cur2 1.29 light chain nucleotide sequence

GATATTGTGATGACTCAGTCTCCACTCTCCCTGCCCGTCACCCCTGGAGAGCCGGCCTCCAT
CTCCTGCAGGTCTAGTCAGAGCCTCCTGCATAGTAATGGATACAACTATTTGGATTGGTACC
TGCAGAAGCCAGGGCAGTCTCCACAACTCCTGATCTATTTGGGTTCTAATCGGGCCTCCGGG
GTCCCTGACAGGTTCAGTGGCAGTGGATCAGGCACAGATTTTACACTGAAAATCAGCAGAGT
GGAGGCTGACGATGTTGGGGTTTATTACTGCATGCAAGCTCTACAATCTCTCATGTGCAGTT
TTGGCCAGGGGACCAAGCTGGAGATCAAAC (SEQ ID NO:72)

D -- Cur2 1.29 light chain protein sequence

DIVMTQSPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQLLIYLGSNRASG
VPDRFSGSGSGTDFTLKISRVEADDVGVYYCMQALQSLMCSFGQGTKLEIK
(SEQ ID NO:30)

FIG. 11

A -- Cur2 1.33 heavy chain nucleotide sequence

CAGGTTCAGCTGGTGCAGTCGGGAGCTGAGGTGAAGAAGCCTGGGGCCTCAGTGAAGGTCTC
CTGCAAGGCTTCTGGTTACACCTTTACCAGCTATGGTATCAGCTGGGTGCGACAGGCCCCTG
GACAAGGGCTTGAGTGGATGGGATGGATCAGCGCTTACAATGGTAACACAAACTATGCACAG
AAGCTCCAGGGCAGAGTCACCATGACCACAGACACATCCACGAGCACAGCCTACATGGAGCT
GAGGAGCCTGAGATCTGACGACACGGCCGTGTATTACTGTGCGAGAGATCATTACTATGATA
GTAGTGATTATCTCTACTACTACTACGGTTTGGACGTCTGGGGCCAAGGGACCACGGTCACC
GTCTCCTCAG (SEQ ID NO:73)

B -- Cur2 1.33 heavy chain protein sequence

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYGISWVRQAPGQGLEWMGWISAYNGNTNYAQ
KLQGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARDHYYDSSDYLYYYYGLDVWGQGTTVT
VSS (SEQ ID NO:31)

C -- Cur2 1.33 light chain nucleotide sequence

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT
CACTTGCCGGGCGAGTCAGGGCATTAGCAATTATTTAGCCTGGTATCAGCAGAAACCAGGGA
AAGTTCCTAAGCTCCTGATCTATGCTGCATCCACTTTGCAATCAGGGGTCCCATCTCGGTTC
AGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGATGT
TGCAACTTATTACTGTCAAAAGTATAACAGTGCCCCGCTCACTTTCGGCGGAGGGACCAAGG
TGGAGATCAAAC (SEQ ID NO:74)

D -- Cur2 1.33 light chain protein sequence

DIQMTQSPSSLSASVGDRVTITCRASQGISNYLAWYQQKPGKVPKLLIYAASTLQSGVPSRF
SGSGSGTDFTLTISSLQPEDVATYYCQKYNSAPLTFGGGTKVEIK (SEQ ID NO:32)

FIG. 12

A -- Cur2 1.38.1 heavy chain nucleotide sequence

CAGGTGCAGCTGGTGGAGTCGGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTC
CTGTGCAGCGTCTGGATTCACCTTCAGTAGCTATGGCATGCACTGGGTCCGCCAGGCTCCAG
GCAAGGGGCTGGAGTGGGTGGCAATTATATGGTATGATGGAAATGATAAATACTATGCAGAC
TCCGTGAAGGGCCGCTTCACCGTCTCCAGAGACAATTCCAAGAACACGCTGTATCTGCAAAT
GAACAGCCTGAGAGCCGAGGACACGGCTGTGTATTACTGTGCGAGAGGATATTACTATGATA
GTAGTGATTATCTCTACTACTACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACC
GTCTCCTCAG (SEQ ID NO:75)

B -- Cur2 1.38.1 heavy chain protein sequence

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAIIWYDGNDKYYAD
SVKGRFTVSRDNSKNTLYLQMNSLRAEDTAVYYCARGYYYDSSDYLYYYYGMDVWGQGTTVT
VSS (SEQ ID NO:33)

C -- Cur2 1.38.1 light chain nucleotide sequence

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT
CACTTGCCGGGCGAGTCAGGGCATTAGCAATTATTTAGCCTGGTATCAGCAGAAACCAGGGA
AAGTTCCTAACCTCCTGATCTATGCTGCATCCACTTTGCAATCAGGGGTCCCATCTCGGTTC
AGTGGCAGTGGATCTGGGACAGATTTCTCTCTCACCATCAGCAGCCTGCAGCCTGAAGATGT
TGCAGCTTATTACTGTCAAAAGTGTAACAGTGCCCCGTGGACGTTCGGCCAAGGGACCACGG
TGGAGATCAAAC (SEQ ID NO:76)

D -- Cur2 1.38.1 light chain protein sequence

DIQMTQSPSSLSASVGDRVTITCRASQGISNYLAWYQQKPGKVPNLLIYAASTLQSGVPSRF
SGSGSGTDFSLTISSLQPEDVAAYYCQKCNSAPWTFGQGTTVEIK (SEQ ID NO:34)

FIG. 13

A -- Cur2 1.39.1 heavy chain nucleotide sequence

GAGGTGCAGCTGGTGCAGTCGGGAACAGAGGTGAAAAAGCCCGGGGAGTCTCTGAAGATCTC
CTGTAAGGGTTCTGGATACAGGTTTACCAGCTACTGGATCGGCTGGGTGCGCCAGATGCCCG
GGAAAGGCCTGGAGTGGATGGGGATCATCTATCCTGGTGACTCTGATACCAGATACAGCCCG
TCCTTCCAAGGCCAGGTCACCATCTCAGCCGACAAGTCCATCAGCACCGCCTACCTGCAGTG
GAGCAGCCTGAAGGCCTCGGACACCGCCATGTATTACTGTGCGAGACATGGATCGTATTACT
ATAATTCGGGGAGTTATTATAACGTCTTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTC
TCCTCAG (SEQ ID NO:77)

B -- Cur2 1.39.1 heavy chain protein sequence

EVQLVQSGTEVKKPGESLKISCKGSGYRFTSYWIGWVRQMPGKGLEWMGIIYPGDSDTRYSP
SFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARHGSYYYNSGSYYNVFDYWGQGTLVTV
SS (SEQ ID NO:35)

C -- Cur2 1.39.1 light chain nucleotide sequence

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT
CACTTGCCGGGCAAGTCAGGGCATTAGAAATGATTTAGGCTGGTATCAGCAGAAACCAGGGA
AAGCCCCTAAGCGCCTGATCTATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTC
AGCGGCAGTGGATCTGGGACAGAATTCACTCTCACAATCAGCAGCCTGCAGCCTGAAGATTT
TGCAACTTATTACTGTCTACAGCATAATAGTTACCCGTGGACGTTCGGCCAAGGGACCAAGG
TGGAAATCAAAC (SEQ ID NO:78)

D -- Cur2 1.39.1 light chain protein sequence

DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPGKAPKRLIYAASSLQSGVPSRF
SGSGSGTEFTLTISSLQPEDFATYYCLQHNSYPWTFGQGTKVEIK (SEQ ID NO:36)

FIG. 14

A -- Cur2 1.40.1 heavy chain nucleotide sequence

CAGGTGCAGCTGGTGCAGTCGGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGTGAAGGTCTC
CTGCAAGGCTTCTGGATACACCTTCACCACTTATGATATCAACTGGGTGCGACAGGCCACTG
GACAAGGGCTTGAGTGGATGGGATGGATGAACCCTAACAGTGGTAACACAGGCTATGCACAG
AAGTTCCAGGGCAGAGTCACCATGACCAGGAACACCTCCCTAAGCACAGCCTACATGGAGCT
GAGCAGCCTGAGATCTGAGGACACGGCCGTGTATTACTGTGCGAGAGATATTGTAGTGGTGG
TAGCTGCTACCAACTACTACAACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTC
TCCTCAG (SEQ ID NO:79)

B -- Cur2 1.40.1 heavy chain protein sequence

QVQLVQSGAEVKKPGASVKVSCKASGYTFTTYDINWVRQATGQGLEWMGWMNPNSGNTGYAQ
KFQGRVTMTRNTSLSTAYMELSSLRSEDTAVYYCARDIVVVVAATNYYNGMDVWGQGTTVTV
SS (SEQ ID NO:37)

FIG. 15

A -- Cur2 1.45 heavy chain nucleotide sequence

CAGGTGCAGCTGGTGCAGTCGGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGTGAAGGTCTC
CTGCAAGGCTTCTGGATACACCTTCACCAGTTATGATATCAACTGGGTGCGACAGGCCACTG
GACAAGGGCTTGAGTGGATGGGATGGATGAACCCTAACAGTGGTAACACAGGCTATGCACAG
AAGTTCCAGGGCAGAGTCACCATGACCAGGAACACCTCCATAAGCACAGCCTACATGGAGCT
GAGCAGCCTGAGATCTGAGGACACGGCCGTGTATTACTGTGCGAGAGGCAGTGGATACAGCT
ATGGTTACGACTACTACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCC
TCAG (SEQ ID NO:80)

B -- Cur2 1.45 heavy chain protein sequence

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDINWVRQATGQGLEWMGWMNPNSGNTGYAQ
KFQGRVTMTRNTSISTAYMELSSLRSEDTAVYYCARGSGYSYGYDYYYGMDVWGQGTTVTVS
S (SEQ ID NO:38)

C -- Cur2 1.45 light chain nucleotide sequence

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT
CAATTGCCGGGCGAGTCAGGGCATTAGCAATGATTTAGCCTGGTATCAGCAGAAACCAGGGA
AAGTTCCTAAGCTCCTGATCTATGCTGCATCCACTTTGCAATTAGGGGTCCCATCTCGGTTC
AGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGATGT
TGCAACTTATTACTGTCAAAAGTATAACAGTGCCCCATTCACTTTCGGCCCTGGGACCAAAG
TGGATATCAAAC (SEQ ID NO:81)

D -- Cur2 1.45 light chain protein sequence

DIQMTQSPSSLSASVGDRVTINCRASQGISNDLAWYQQKPGKVPKLLIYAASTLQLGVPSRF
SGSGSGTDFTLTISSLQPEDVATYYCQKYNSAPFTFGPGTKVDIK (SEQ ID NO:39)

FIG. 16

A -- Cur2 1.46.1 heavy chain nucleotide sequence

CAGGTGCAGCTGGTGCAGTCGGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGTGAAGGTCTC
CTGCAAGGCTTCTGGATACTCCTTCACCAGTTATGATATCAACTGGGTGCGACAGGCCACTG
GACAAGGGCTTGAGTGGATGGGATGGATGAACCCTAACAATGGTAACACAGGCTATGCACAG
AAGTTCCAGGGCAGAGTCACCATGACCAGGAACACCTCCATAAGCACAGCCTACATGGAGCT
GAGCAGCCTGAGATCTGAGGACACGGCCGTGTATTACTGTGCGAGAGATATTGTAGTGGTGG
TAACTGCTACGGACTACTACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTC
TCCTCAG (SEQ ID NO:82)

B -- Cur2 1.46.1 heavy chain protein sequence

QVQLVQSGAEVKKPGASVKVSCKASGYSFTSYDINWVRQATGQGLEWMGWMNPNNGNTGYAQ
KFQGRVTMTRNTSISTAYMELSSLRSEDTAVYYCARDIVVVVTATDYYYGMDVWGQGTTVTV
SS (SEQ ID NO:40)

C -- Cur2 1.46.1 light chain nucleotide sequence

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT
CACTTGCCGGGCAAGTCAGGGCATTAGAAATGATTTAGGCTGGTATCAGCAGAAACCAGGGA
AAGCCCCTAAGCGCCTGATTTTTGCTGCATCCAGTTTGCCAAGTGGGGTCCCATCAAGGTTC
AGCGGCAGTGGATCTGGGACAGAATTCACTCTCACAATCAGCAGCCTGCAGCCTGAAGATTT
TGCAACTTATTACTGTCTACAGCATAGTGGTTACCCTCCGACGTTCGGCCAAGGGACCAAGG
TGGAAATCAAAC (SEQ ID NO:83)

D -- Cur2 1.46.1 light chain protein sequence

DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPGKAPKRLIFAASSLPSGVPSRF
SGSGSGTEFTLTISSLQPEDFATYYCLQHSGYPPTFGQGTKVEIK (SEQ ID NO:41)

FIG. 17

A -- Cur2 1.48.1 heavy chain nucleotide sequence

CAGGTTCAGCTGGTGCAGTCGGGAGCTGAGGTGAAGAAGCCTGGGGCCTCAGTGAAGGTCTC
CTGCAAGGCTTCTGGTTACACCTTTACCAGCTATGGTATCAGCTGGGTGCGACAGGCCCCTG
GACAAGGGCTTGAGTGGATGGGATGGATCAGCGCTTACAATGGTAACACAAACTATGCACAG
AAGCTCCAGGGCAGAGTCACCATGACCACAGACACATCCACGAGCACAGCCTACATGGAGCT
GAGGAGCCTGAGATCTGACGACACGGCCGTGTATTACTGTGCGAGAGATGTTGAATATTACT
ATGATGGTAGTGGTTATTACTACTTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTCC
TCAG (SEQ ID NO:84)

B -- Cur2 1.48.1 heavy chain protein sequence

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYGISWVRQAPGQGLEWMGWISAYNGNTNYAQ
KLQGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARDVEYYYDGSGYYYFDYWGQGTLVTVS
S (SEQ ID NO:42)

C -- Cur2 1.48.1 light chain nucleotide sequence

GACATCCAGATGACCCAGTCTCCATCTTCCGTGTCTGCATCTGTAGGAGACAGAGTCACCAT
CACTTGTCGGGCGAGTCAGGGTATTAGCAGCTGGTTAGCCTGGTATCAGCAGAAACCAGGGA
AAGCCCCTAAGCTCCTGATCTATGCTGCATCCATTTTGCAAAGTGGGGTCCCATCAAGGTTC
AGCGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGCCTGCAGCCTGAGGATTT
TGCATCTTACTATTGTCAACAGTCTAACAGTTTCCCTCGGACGTTCGGCCAAGGGACCAAGG
TGGAGATCAAAC (SEQ ID NO:85)

D -- Cur2 1.48.1 light chain protein sequence

DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIYAASILQSGVPSRF
SGSGSGTDFTLTISSLQPEDFASYYCQQSNSFPRTFGQGTKVEIK (SEQ ID NO:43)

FIG. 18

A -- Cur2 1.49.1 heavy chain nucleotide sequence

CAGGTGCAGCTGGTGCAGTCGGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGTGAAGGTCTC
CTGCAAGGCTTCTGGATACACCTTCACCAGTTATGATATCAACTGGGTGCGACAGGCCACTG
GACAAGGGCTTGAGTGGATGGGATGGATGAACCCTAACAGTGGTGACACAGGCTATGCACAG
AAGTTCCAGGGCAGAGTCACCATGACCAGGAACACCTCCATAAGCACAGCCTACATGGAGCT
GAGCAGCCTGAGATCTGAGGACACGGCCGTGTATTTCTGTGCGAGAATGAGGGATATAGTGG
CTACGAGCTATTACTACTACTTCTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACC
GTCTCCTCAG (SEQ ID NO:86)

B -- Cur2 1.49.1 heavy chain protein sequence

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDINWVRQATGQGLEWMGWMNPNSGDTGYAQ
KFQGRVTMTRNTSISTAYMELSSLRSEDTAVYFCARMRDIVATSYYYYFYGMDVWGQGTTVT
VSS (SEQ ID NO:44)

C -- Cur2 1.49.1 light chain nucleotide sequence

GATATTGTGATGACTCAGTCTCCACTCTCCCTGCCCGTCACCCCTGGAGAGCCGGCCTCCAT
CTCCTGCAGGTCTAGTCAGAGCCTCCTGCATAGTAATGGATACAACTATTTGGATTGGTACC
TGCTGAAGCCAGGGCAGTCTCCACAGCTCCTGATCTATTTGGGTTCTAGTCGGGCCTCCGGG
GTCCCTGACAGGTTCAGTGGCAGTGGATCAGGCACAGATTTTACACTGAAAATCAGCAGAGT
GGAGGCTGAGGATGTTGGGGTTTATTACTGCATGCAAACTCTACAAACTATCACCTTCGGCC
AAGGGACACGACTGGAGATTAAAC (SEQ ID NO:87)

D -- Cur2 1.49.1 light chain protein sequence

DIVMTQSPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLLKPGQSPQLLIYLGSSRASG
VPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQTLQTITFGQGTRLEIK
(SEQ ID NO:45)

FIG. 19

A -- Cur2 1.51 heavy chain nucleotide sequence

GAGGTGCAGCTGGTGCAGTCGGGAGCTGAGGTGAAAAAGCCCGGGGAGTCTCTGAAGATCTC
CTGTAAGGGTTCTGGATACAGCTTTACCAGCTACTGGATCGGCTGGGTGCGCCAGATGCCCG
GGAAAGGCCTGGAGTGGATGGGGATCATCTATCCTGGTGACTCTGATGCCAAATACAGCCCG
TCCTTCCAAGGCCAGGTCACCATCTCAGCCGACAAGTCCATCAGCACCGCCTACCTGCAGTG
GAGCAGCCTGAAGGCCTCGGACACCGCCATGTATTACTGTGCGAGACACTATGATTACGTTT
GGAGGAATTATCGGTATACAGGGTGGTTCGACCCCTGGGGCCAGGGAACCCTGGTCACCGTC
TCCTCAG (SEQ ID NO:88)

B -- Cur2 1.51.1 heavy chain protein sequence

EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGIIYPGDSDAKYSP
SFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARHYDYVWRNYRYTGWFDPWGQGTLVTV
SS (SEQ ID NO:46)

C -- Cur2 1.51.1 light chain nucleotide sequence

GAAATTGTGTTGACGCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGAAAGAGCCACCCT
CTCCTGCAGGGCCAGTCAGAGTGTTAGCAGCAGCTACTTAGCCTGGTACCAGCAGAAACCTG
GCCAGGCTCCCAGGCTCCTCATCTATGGTGCATCCAACAGGGCCACTGGCATCCCAGACAGG
TTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAGACTGGAGCCTGAAGA
TTTTGCAGTGTATTACTGTCAGCAGTATGGTAGCTCACTATTCACTTTCGGCCCTGGGACCA
AAGTGGATATCAAAC (SEQ ID NO:89)

D -- Cur2 1.51.1 light chain protein sequence

EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASNRATGIPDR
FSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSLFTFGPGTKVDIK (SEQ ID NO:47)

FIG. 20

A -- Cur2 6.4 heavy chain nucleotide sequence

CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGTGAAGGTCTC
CTGCAAGGCTTCTGGATACACCTTCACCAGTTATGATATCAACTGGGTGCGACAGGCCACTG
GACAAGGGCTTGAGTGGATGGGATGGATAAACCCTAATAGTGGTAACACAGACTATGCACAG
AAGTTCCAGGGCAGAGTCACCATGACCAGGGACACCTCCATAAGCACAGCCTACATGGAGCT
GAGCAGCCTGAGATCTGAGGACACGGCCATATATTATTGTGTGAGAGGCTTTGGATACAGCT
ATAATTACGACTACTATTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCC
TCAGT (SEQ ID NO:90)

B -- Cur2 6.4 heavy chain amino acid sequence

QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDINWVRQATGQGLEWMGWINPNSGNTDYAQ
KFQGRVTMTRDTSISTAYMELSSLRSEDTAIYYCVRGFGYSYNYDYYYGMDVWGQGTTVTVS
S (SEQ ID NO:48)

C -- Cur2 6.4 light chain nucleotide sequence

GAAATTGTGTTGACGCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGAAAGAGCCACCCT
CTCCTGCAGGGCCAGTCAGAGTGTTAGTAGTAGTTACTTAGCCTGGTACCAGCAGAAGCCTG
GCCAGGCTCCCAGGCTCCTCATCTATGCTACATCCAGCAGGGCCACTGGCATCCCAGACAGG
TTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAGACTGGAGCCTGAAGA
TTTTGCAGTGTATTACTGTCAGCAGTATGGTAGTTCACCGTGCAGTTTTGGCCAGGGGACCA
AGCTGGAAATCAAGC (SEQ ID NO:91)

D -- Cur2 6.4 light chain amino acid sequence

EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYATSSRATGIPDR
FSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSPCSFGQGTKLEIK (SEQ ID NO:49)

FIG. 21

Clone	Germline genes used				No. of Nucleotide/ Amino acid changes						
					FR1	CDR1	FR2	CDR2	FR3	CDR3	FR4
CR2		V	D	J	V					D & J	
1.19.1	VH	V1-8	D3-16	JH6B	0/0	0/0	0/0	0/0	0/0	0/0	0/0
	VK	A30		JK2	0/0	0/0	0/0	0/0	1/1	1/1	0/0
6.4.1	VH	V1-8	D5-18	JH6B	0/0	0/0	0/0	3/2	5/3	0/0	0/0
	VK	A27		JK2	0/0	3/0	1/0	2/2	0/0	1/0	0/0
1.18	VH	V1-8	D6-19	JH6B	1/0	0/0	0/0	1/0	0/0	0/0	0/0
	VK	A30		JK3	0/0	0/0	0/0	0/0	1/1	0/0	0/0
1.40.1	VH	V1-8	D2	JH6B	1/0	1/1	0/0	0/0	1/1	0/0	0/0
	VK	mix									
1.45	VH	V1-8	DK4	JH6B	1/0	0/0	0/0	0/0	0/0	0/0	0/0
	VK	A20		JK3	1/1	1/1	0/0	1/1	0/0	0/0	0/0
1.46.1	VH	V1-8	D2	JH6B	1/0	1/1	0/0	0/0	1/1	0/0	0/0
	VK	A30		JK1	0/0	0/0	2/1	1/1	0/0	2/2	0/0
1.49.1	VH	V1-8	D5-12	JH6B	1/0	0/0	0/0	1/1	1/1	0/0	0/0
	VK	A19		JK5	0/0	0/0	1/1	1/1	0/0	1/1	0/0
1.33	VH	V1-18	D21-9	JH6B	1/0	0/0	0/0	0/0	0/0	0/0	0/0
	VK	A20		JK4	0/0	0/0	0/0	0/0	0/0	0/0	0/0
1.48.1	VH	V1-18	D21-9	JH4B	1/0	0/0	0/0	0/0	0/0	0/0	0/0
	VK	L5		JK1	0/0	0/0	0/0	1/1	2/1	1/1	0/0
1.6.1	VH	V3-21	D3-16	JH4B	0/0	4/4	0/0	1/1	1/0	0/0	0/0
	VK	A30		JK4	0/0	0/0	1/1	0/0	0/0	0/0	0/0
1.17.1	VH	V3-33	D5-18	JH6B	2/1	0/0	0/0	0/0	0/0	0/0	0/0
	VK	A30		JK4	0/0	0/0	0/0	0/0	0/0	0/0	0/0
1.24.1	VH	V3-33	D5-18	JH6B	0/0	2/1	0/0	1/1	0/0	0/0	0/0
	VK	A30		JK1	0/0	0/0	0/0	0/0	1/0	0/0	0/0
1.38.1	VH	V3-33	D21-9	JH6B	1/0	0/0	0/0	3/3	2/1	0/0	0/0
	VK	A20		JK1	0/0	0/0	1/1	0/0	2/2	1/1	0/0
1.11.1	VH	V3-53	D4-17	JH6B	0/0	0/0	0/0	0/0	0/0	0/0	0/0
	VK	A19		JK4	0/0	1/1	0/0	0/0	0/0	0/0	0/0
1.23.1	VH	V5-51	D3-10	JH4B	1/1	0/0	0/0	0/0	0/0	0/0	0/0
	VK	A30		JK1	0/0	0/0	1/1	1/1	0/0	0/0	0/0
1.25.1	VH	V5-51	D3-10	JH4B	1/0	1/1	0/0	0/0	0/0	0/0	0/0
	VK	A30		JK1	0/0	0/0	0/0	0/0	0/0	0/0	0/0
1.29	VH	V5-51	D5-12	JH6B	1/0	0/0	0/0	0/0	1/1	0/0	0/0
	VK	A19		JK2	0/0	0/0	1/0	0/0	1/1	0/0	0/0
1.39.1	VH	V5-51	D3-10	JH4B	2/1	1/1	0/0	0/0	0/0	0/0	0/0
	VK	A30		JK1	0/0	0/0	0/0	0/0	0/0	0/0	0/0
1.51.1	VH	5-51	D3-16	JH5B	2/0	0/0	0/0	1/1	1/1	0/0	0/0
	VK	A27		JK3	0/0	0/0	0/0	1/1	0/0	0/0	0/0

FIG. 22A

Clone	Germline genes used				No. of Nucleotide/ Amino acid changes						
					FR1	CDR1	FR2	CDR2	FR3	CDR3	FR4
CR2		V	D	J	V					D & J	
1.40.1	VH	V1-8	D2	JH6B	1/0	1/1	0/0	0/0	1/1	0/0	0/0
	VK	mix									
1.48.1	VH	V1-18	D21-9	JH4B	1/0	0/0	0/0	0/0	0/0	0/0	0/0
	VK	L5		JK1	0/0	0/0	0/0	1/1	2/1	1/1	0/0
1.49.1	VH	V1-8	D5-12	JH6B	1/0	0/0	0/0	1/1	1/1	0/0	0/0
	VK	A19		JK5	0/0	0/0	1/1	1/1	0/0	1/1	0/0
1.11.1	VH	V3-53	D4-17	JH6B	0/0	0/0	0/0	0/0	0/0	0/0	0/0
	VK	A19		JK4	0/0	1/1	0/0	0/0	0/0	0/0	0/0
1.29	VH	V5-51	D5-12	JH6B	1/0	0/0	0/0	0/0	1/1	0/0	0/0
	VK	A19		JK2	0/0	0/0	1/0	0/0	1/1	0/0	0/0
1.45	VH	V1-8	DK4	JH6B	1/0	0/0	0/0	0/0	0/0	0/0	0/0
	VK	A20		JK3	1/1	1/1	0/0	1/1	0/0	0/0	0/0
1.33	VH	V1-18	D21-9	JH6B	1/0	0/0	0/0	0/0	0/0	0/0	0/0
	VK	A20		JK4	0/0	0/0	0/0	0/0	0/0	0/0	0/0
1.38.1	VH	V3-33	D21-9	JH6B	1/0	0/0	0/0	3/3	2/1	0/0	0/0
	VK	A20		JK1	0/0	0/0	1/1	0/0	2/2	1/1	0/0
6.4.1	VH	V1-8	D5-18	JH6B	0/0	0/0	0/0	3/2	5/3	0/0	0/0
	VK	A27		JK2	0/0	3/0	1/0	2/2	0/0	1/0	0/0
1.51.1	VH	5-51	D3-16	JH5B	2/0	0/0	0/0	1/1	1/1	0/0	0/0
	VK	A27		JK3	0/0	0/0	0/0	1/1	0/0	0/0	0/0
1.19.1	VH	V1-8	D3-16	JH6B	0/0	0/0	0/0	0/0	0/0	0/0	0/0
	VK	A30		JK2	0/0	0/0	0/0	0/0	1/1	1/1	0/0
1.18	VH	V1-8	D6-19	JH6B	1/0	0/0	0/0	1/0	0/0	0/0	0/0
	VK	A30		JK3	0/0	0/0	0/0	0/0	1/1	0/0	0/0
1.6.1	VH	V3-21	D3-16	JH4B	0/0	4/4	0/0	1/1	1/0	0/0	0/0
	VK	A30		JK4	0/0	0/0	1/1	0/0	0/0	0/0	0/0
1.23.1	VH	V5-51	D3-10	JH4B	1/1	0/0	0/0	0/0	0/0	0/0	0/0
	VK	A30		JK1	0/0	0/0	1/1	1/1	0/0	0/0	0/0
1.25.1	VH	V5-51	D3-10	JH4B	1/0	1/1	0/0	0/0	0/0	0/0	0/0
	VK	A30		JK1	0/0	0/0	0/0	0/0	0/0	0/0	0/0
1.39.1	VH	V5-51	D3-10	JH4B	2/1	1/1	0/0	0/0	0/0	0/0	0/0
	VK	A30		JK1	0/0	0/0	0/0	0/0	0/0	0/0	0/0
1.17.1	VH	V3-33	D5-18	JH6B	2/1	0/0	0/0	0/0	0/0	0/0	0/0
	VK	A30		JK4	0/0	0/0	0/0	0/0	0/0	0/0	0/0
1.24.1	VH	V3-33	D5-18	JH6B	0/0	2/1	0/0	1/1	0/0	0/0	0/0
	VK	A30		JK1	0/0	0/0	0/0	0/0	1/0	0/0	0/0
1.46.1	VH	V1-8	D2	JH6B	1/0	1/1	0/0	0/0	1/1	0/0	0/0
	VK	A30		JK1	0/0	0/0	2/1	1/1	0/0	2/2	0/0

FIG. 22B

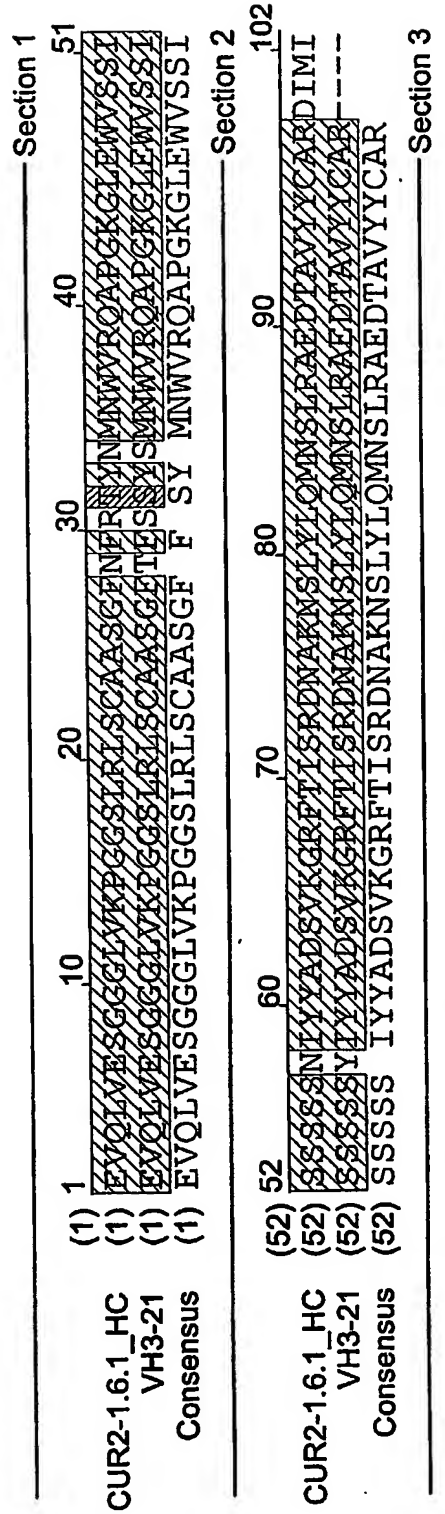


FIG. 23A

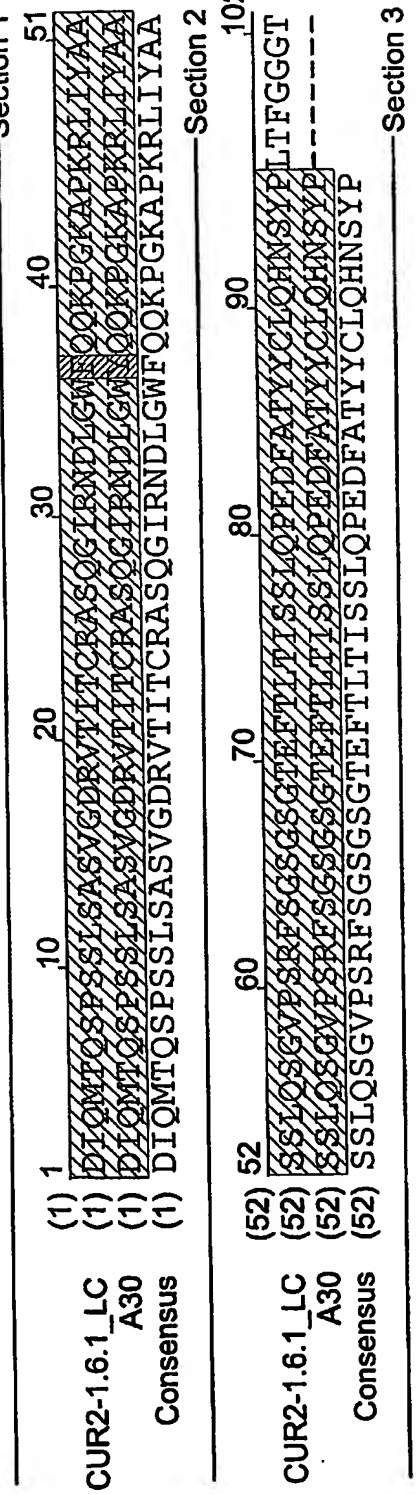

Section 1
Section 2
Section 3
CUR2-1.6.1_LC
A30
Consensus
DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWFQQKPGKAPKRLIYAA
KVEIK

FIG. 23B

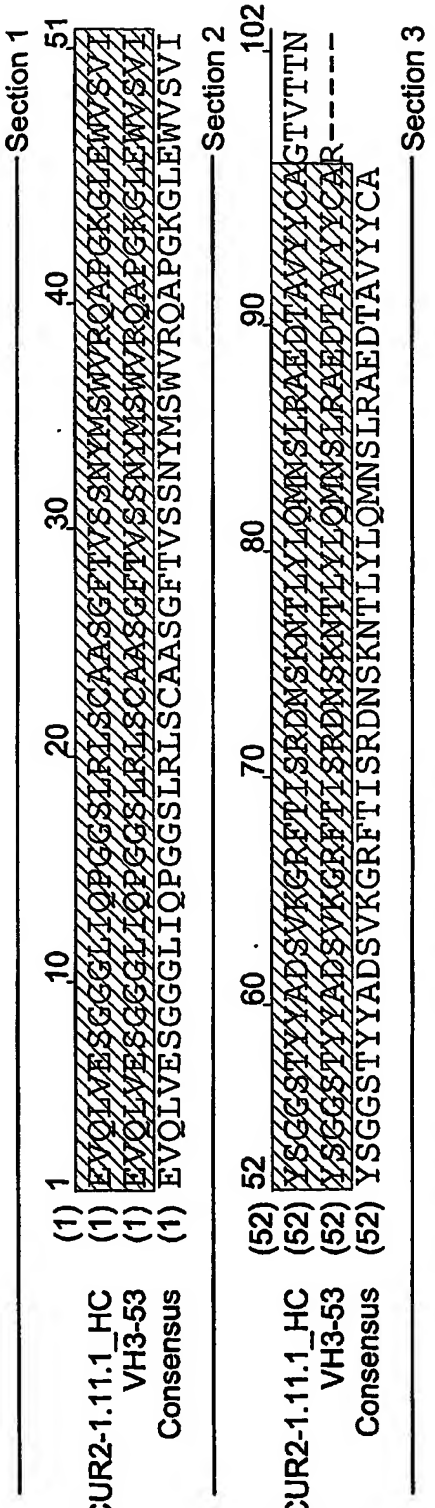

Section 1
Section 2
Section 3
CUR2-1.11.1_HC
VH3-53
Consensus
EVQLVESGGGLIQPGGSLRLSCAASGFTVSSNYMSWVRQAPGKGLEWVSVI
YYYGMDVWGQGTTVTVSS

FIG. 24A

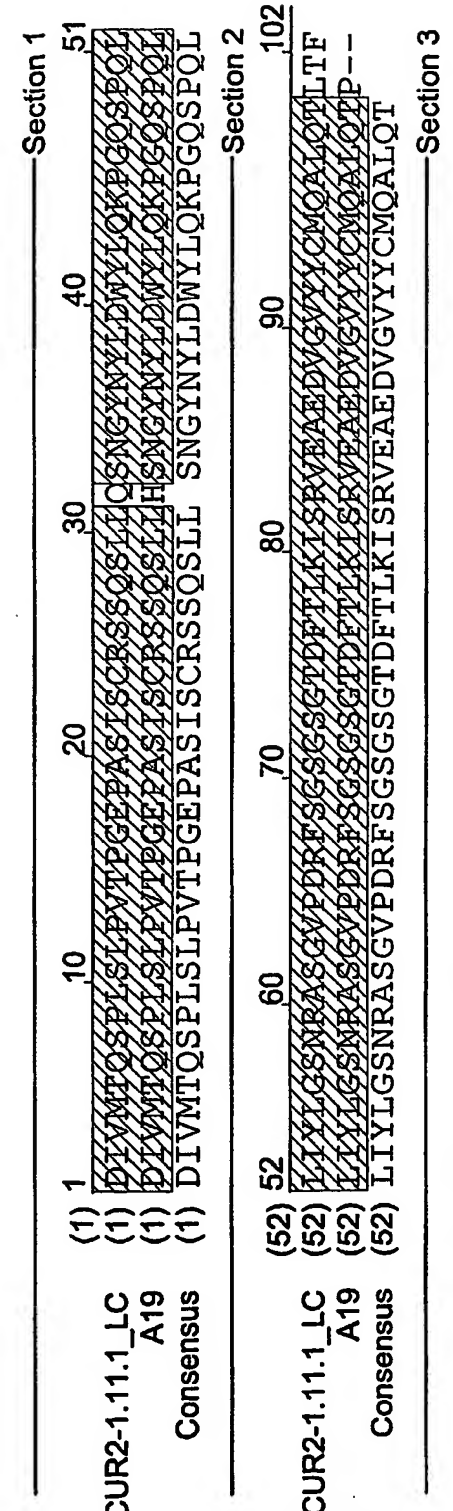

Section 1
Section 2
Section 3
CUR2-1.11.1_LC
A19
Consensus
DIVMTQSPLSLPVTPGEPASISCRSSQSLLQSNGYNYLDWYLQKPGQSPQL
SNGYNYLDWYLQKPGQSPQL
LIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQT
GGGTKVEIK

FIG. 24B

Section 1
Section 2
Section 3
CR2-1.17.1_HC
VH3-33
Consensus
QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVI
QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVI
QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVI
WYDGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR
WYDGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR
WYDGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR
RYAGYYYDYGMDVWGQGTTVTVSS

FIG. 25A

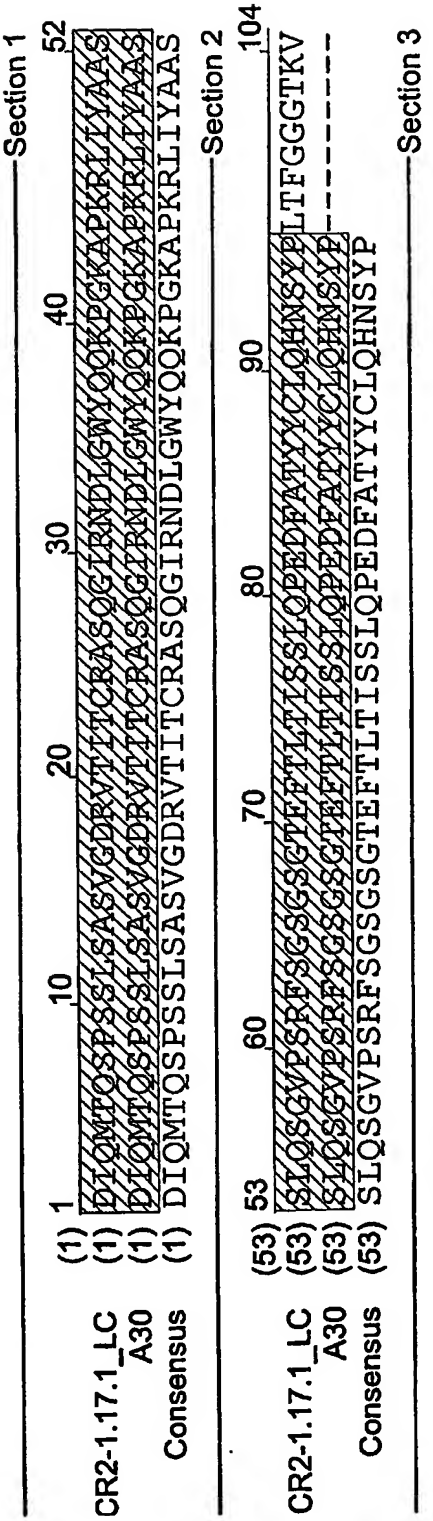

Section 1
Section 2
Section 3
CR2-1.17.1_LC
A30
Consensus
DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPGKAPKRLIYAAS
SLQSGVPSRFSGSGSGTEFTLTISSLQPEDFATYYCLQHNSYPLTFGGGTKV
EIK

FIG. 25B

Section 1
Section 2
Section 3
CR2-1.18_HC
VH1-8
Consensus
VH31-8
Cons nsus
QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDINWVRQATGQGLEWMGWMN
PNSGNTGYAQKFQGRVTMTRNTSISTAYMELSSLRSEDTAVYYCAR
EGIAVA
GTYYYYYGMDVWGQGTTVTVSS

FIG. 26A

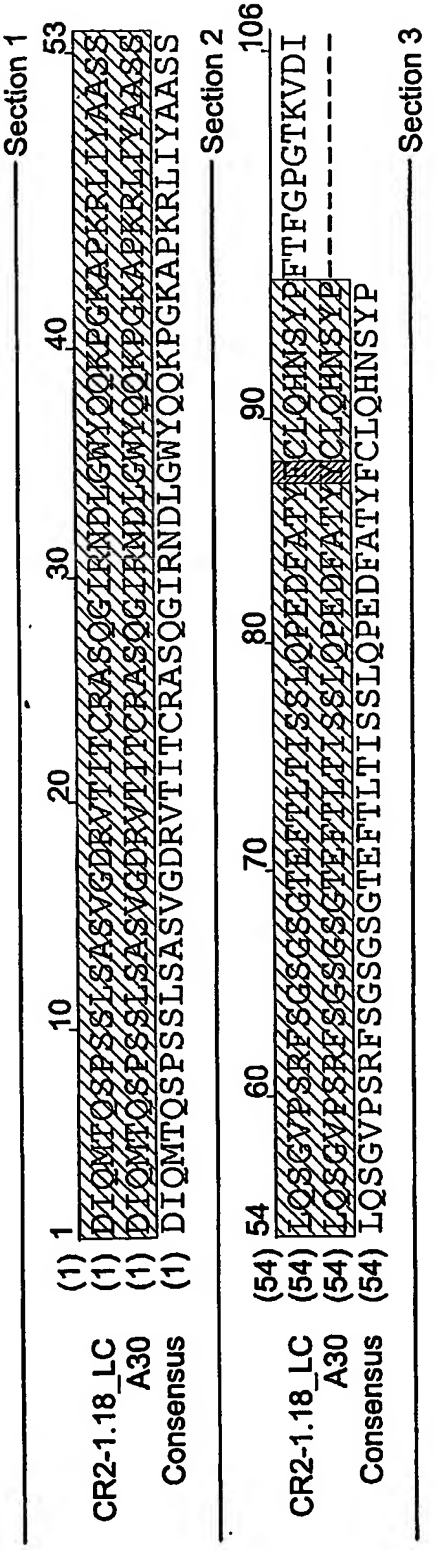

Section 1
CR2-1.18_LC (1) DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPGKAPKRLIYAASS
A30 (1) DIQMTQSPSSLSASVGDRVTITCRASQGIRMDLGWYQQKPGKAPKRLIYAASS
Consensus (1) DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPGKAPKRLIYAASS
Section 2
CR2-1.18_LC (54) LQSGVPSRFSGSGSGTEFTLTISSLQPEDFATYYCLQHNSYPFTFGPGTKVDI
A30 (54) LQSGVPSRFSGSGSGTEFTLTISSLQPEDFATYYCLQHNSYP----------
Consensus (54) LQSGVPSRFSGSGSGTEFTLTISSLQPEDFATYFCLQHNSYP
Section 3
CR2-1.18_LC (107) K
A30 (96) -
Consensus (107)

FIG. 26B

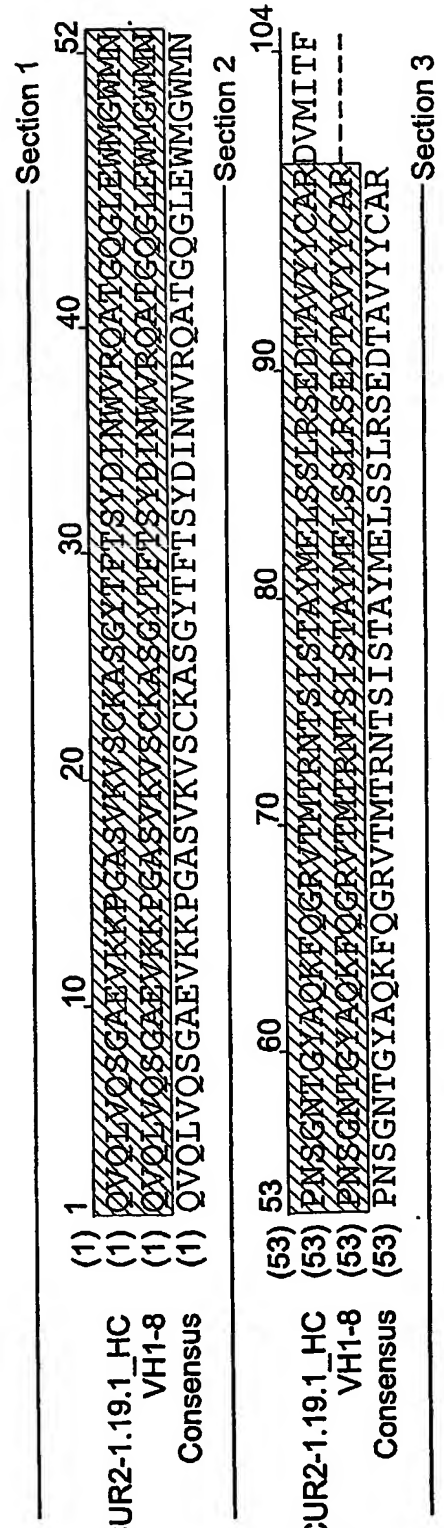

Section 1
Section 2
Section 3
CUR2-1.19.1_HC
VH1-8
Consensus
CUR2-1.19.1_HC
VH1-8
Consensus
CUR2-1.19.1_HC
VH31-8
Consensus
QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDINWVRQATGQGLEWMGWMN
QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDINWVRQATGQGLEWMGWMN
QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDINWVRQATGQGLEWMGWMN
PNSGNTGYAQKFQGRVTMTRNTSISTAYMELSSLRSEDTAVYYCAR
PNSGNTGYAQKFQGRVTMTRNTSISTAYMELSSLRSEDTAVYYCAR
PNSGNTGYAQKFQGRVTMTRNTSISTAYMELSSLRSEDTAVYYCAR
GGVIVHYGMDVWGQGTTVTVSS

FIG. 27A

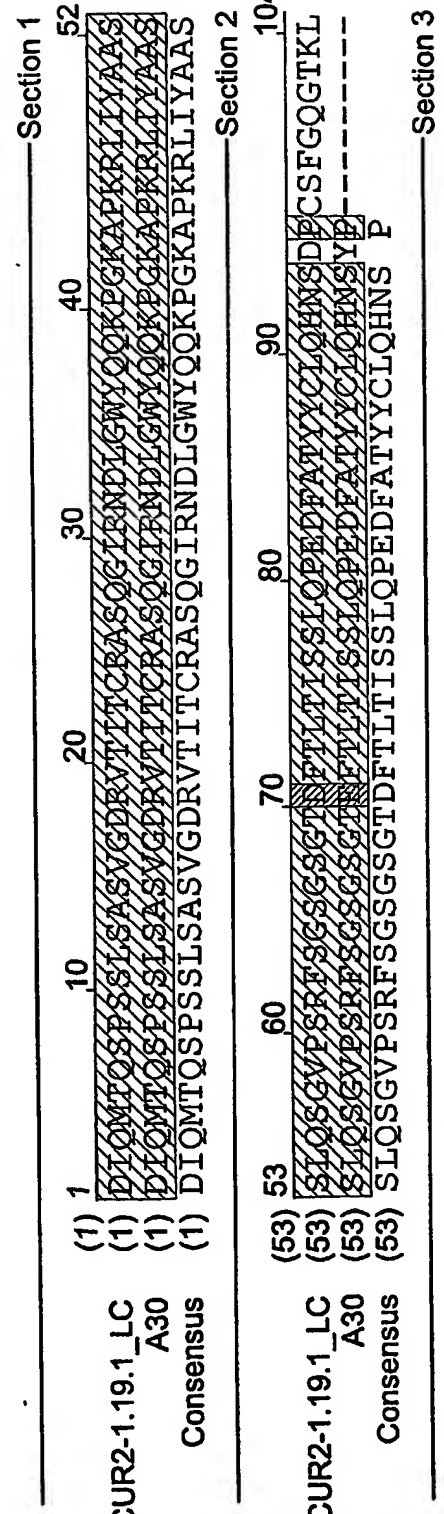

Section 1
Section 2
Section 3
CUR2-1.19.1_LC
A30
Consensus
DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPGKAPKRLIYAAS
SLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCLQHNSYP
EIR

FIG. 27B

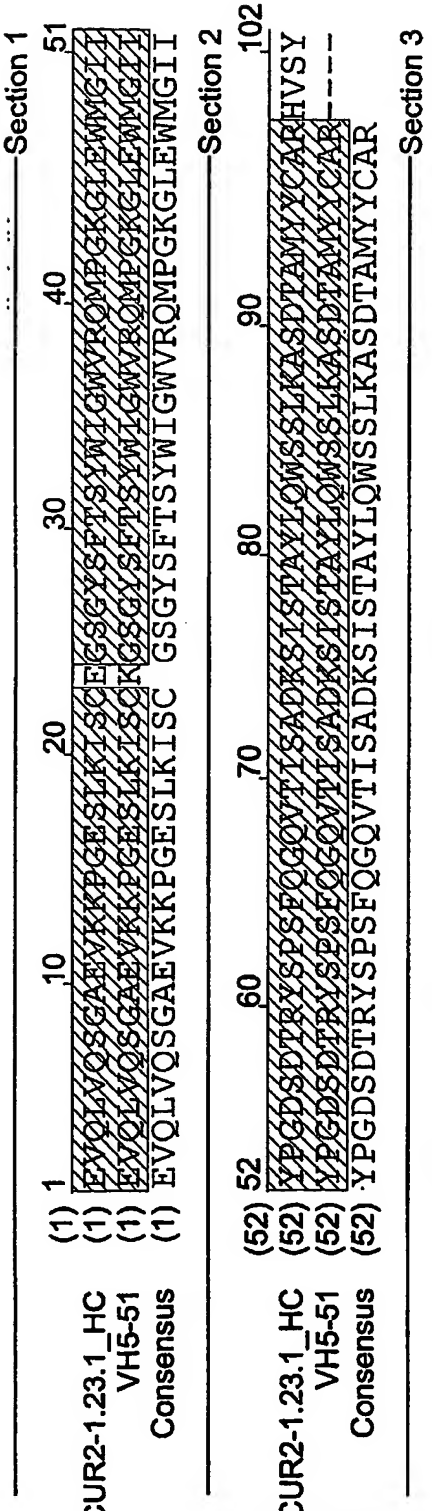

Section 1
Section 2
Section 3
CUR2-1.23.1_HC
VH5-51
Consensus
EVQLVQSGAEVKKPGESLKISC GSGYSFTSYWIGWVRQMPGKGLEWMGII
YPGDSDTRYSPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCAR
YYVSGSYYNVFDYWGQGTLVTVSS

FIG. 28A

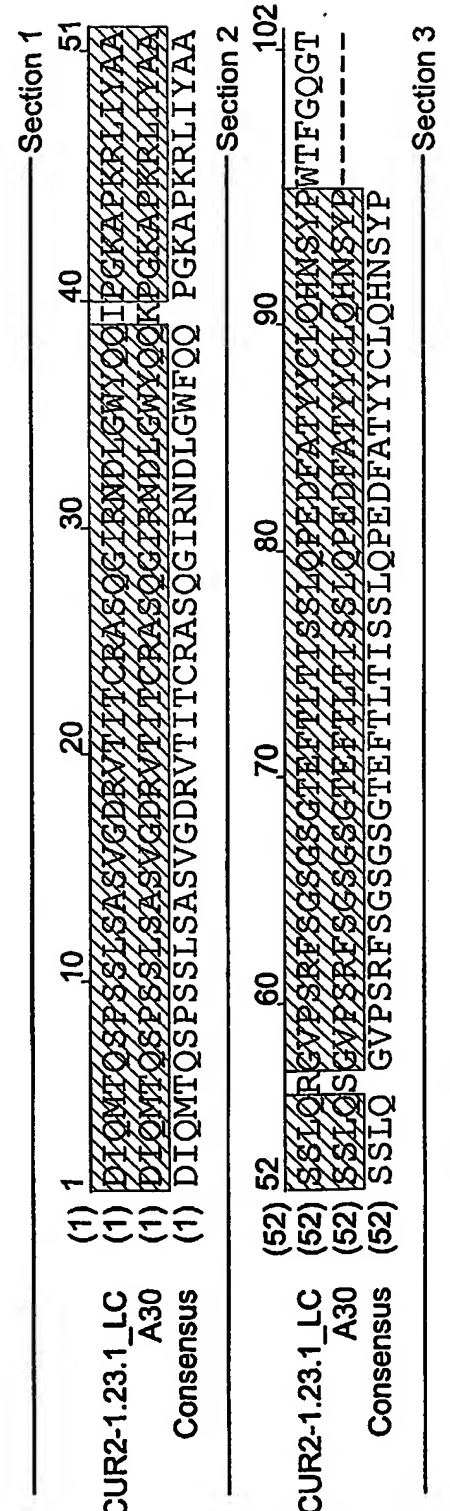

Section 1
Section 2
Section 3
CUR2-1.23.1_LC
A30
Consensus
DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQIPGKAPKRLIYAA
SSLQ GVPSRFSGSGSGTEFTLTISSLQPEDFATYYCLQHNSYP
KVEIK

FIG. 28B

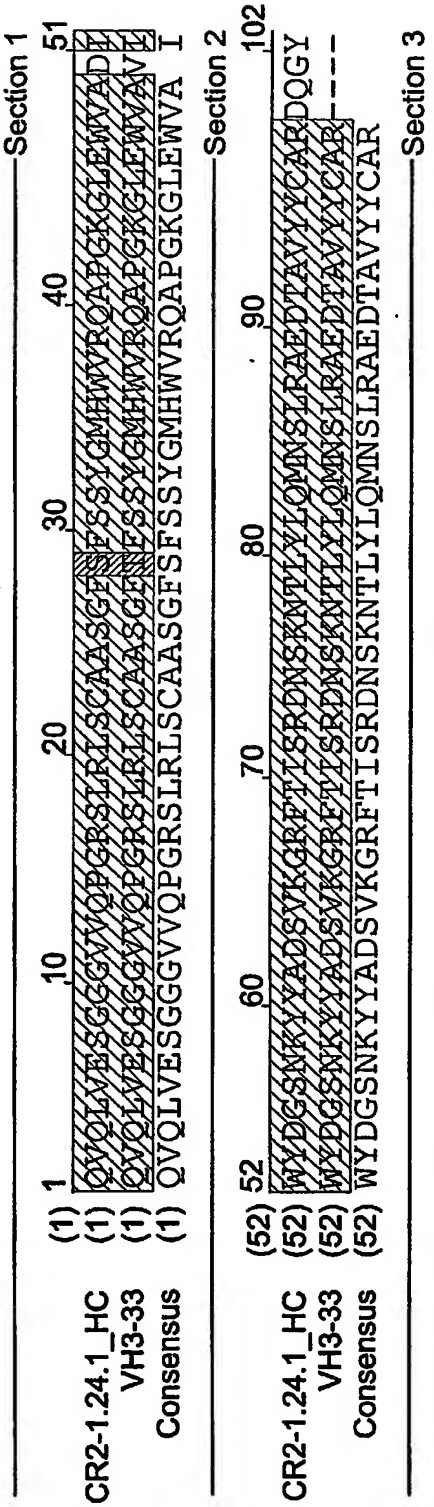

Section 1
Section 2
Section 3
CR2-1.24.1_HC
VH3-33
Consensus
QVQLVESGGGVVQPGRSLRLSCAASGFSFSSYGMHWVRQAPGKGLEWVADQGY
QVQLVESGGGVVQPGRSLRLSCAASGFSFSSYGMHWVRQAPGKGLEWVAV----
QVQLVESGGGVVQPGRSLRLSCAASGFSFSSYGMHWVRQAPGKGLEWVA
WYDGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR
WYDGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR
WYDGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR
SYGYVYYDYGMDVWGQGTTVTVSS

FIG. 29A

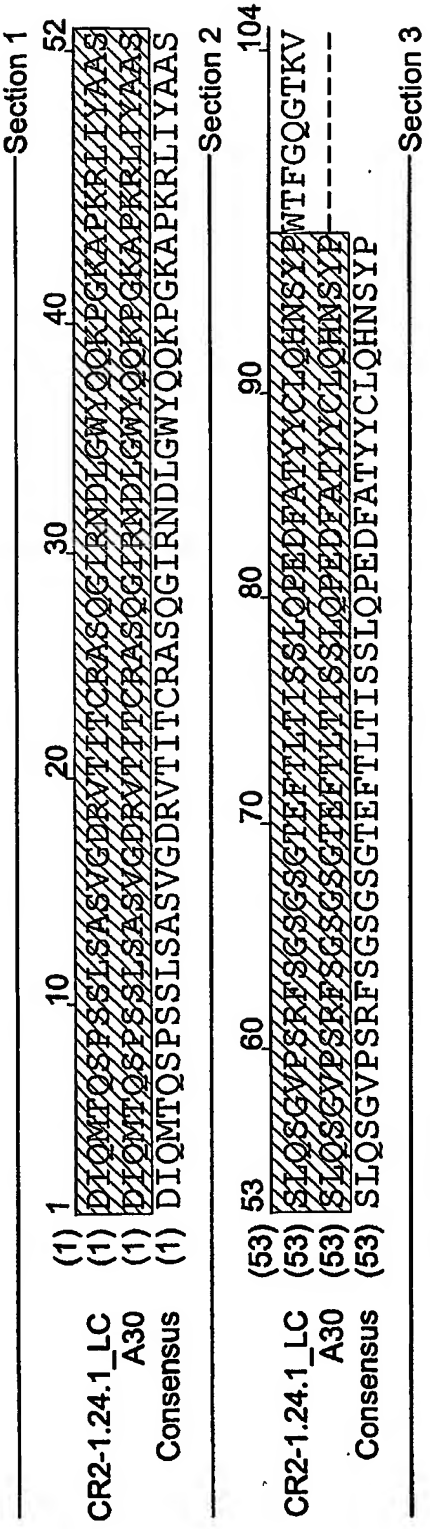

Section 1
Section 2
Section 3
CR2-1.24.1_LC
A30
Consensus
(1) 1 10 20 30 40 52
(1) DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPGKAPKRLIYAAS
(1) DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPGKAPKRLIYAAS
(1) DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPGKAPKRLIYAAS
(53) 53 60 70 80 90 104
(53) SLQSGVPSRFSGSGSGTEFTLTISSLQPEDFATYYCLQHNSYPWTFGQGTKV
(53) SLQSGVPSRFSGSGSGTEFTLTISSLQPEDFATYYCLQHNSYP----------
(53) SLQSGVPSRFSGSGSGTEFTLTISSLQPEDFATYYCLQHNSYP
(105) 105107
(105) EIK
(96) ---
(105)

FIG. 29B

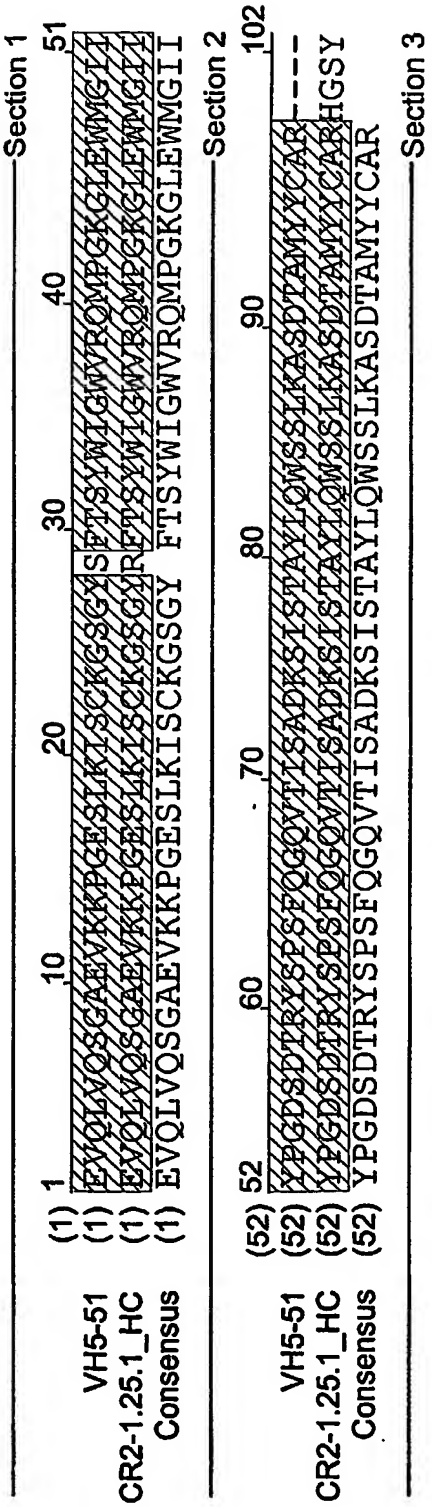

Section 1
Section 2
Section 3
VH5-51
CR2-1.25.1_HC
Consensus
EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGII
YYGSETYYNVFDYWGQGTLVTVSS

FIG. 30A

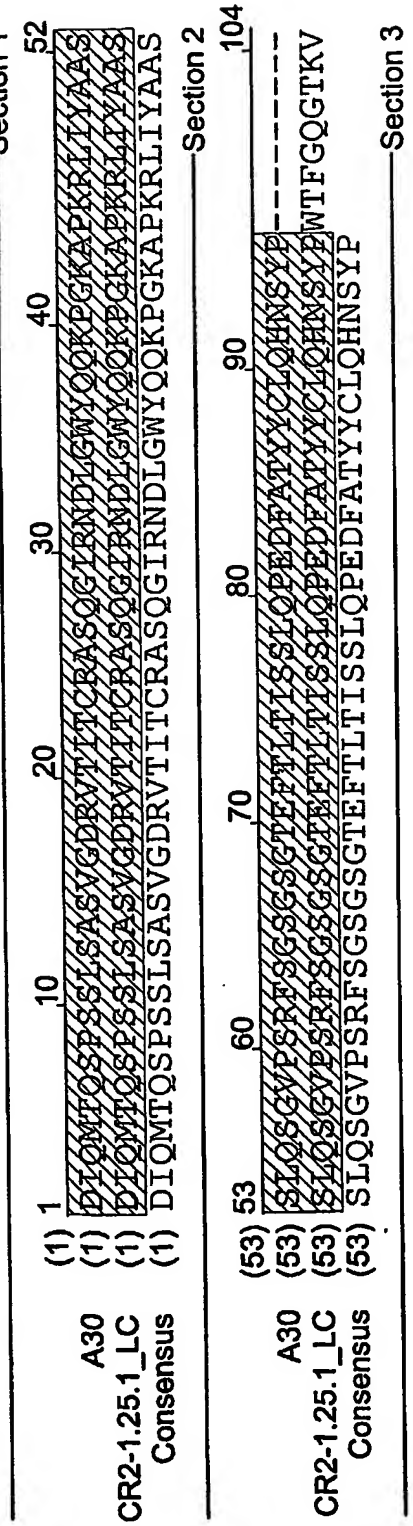

Section 1
Section 2
Section 3
A30
CR2-1.25.1_LC
Consensus
(1) 1
(1) 10
(1) 20
(1) 30
(1) 40
(1) 52
(1) DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPGKAPKRLIYAAS
(53) 53
(53) 60
(53) 70
(53) 80
(53) 90
(53) 104
(53) SLQSGVPSRFSGSGSGTEFTLTISSLQPEDFATYYCLQHNSYP
(105) 105107
(96) ---
(105) EIK
(105)

FIG. 30B

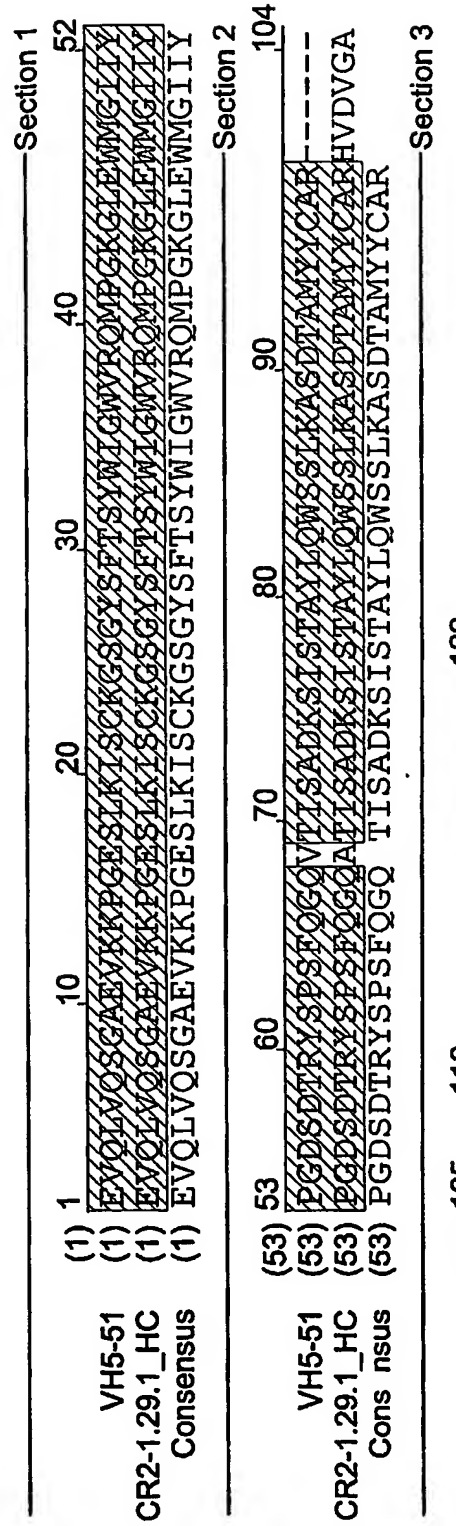

Section 1
Section 2
Section 3
VH5-51
CR2-1.29.1_HC
Consensus
EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGIIY
PGDSDTRYSPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCAR
TIGGYYYYYHGMDVWGQGTTVTVSS

FIG. 31A

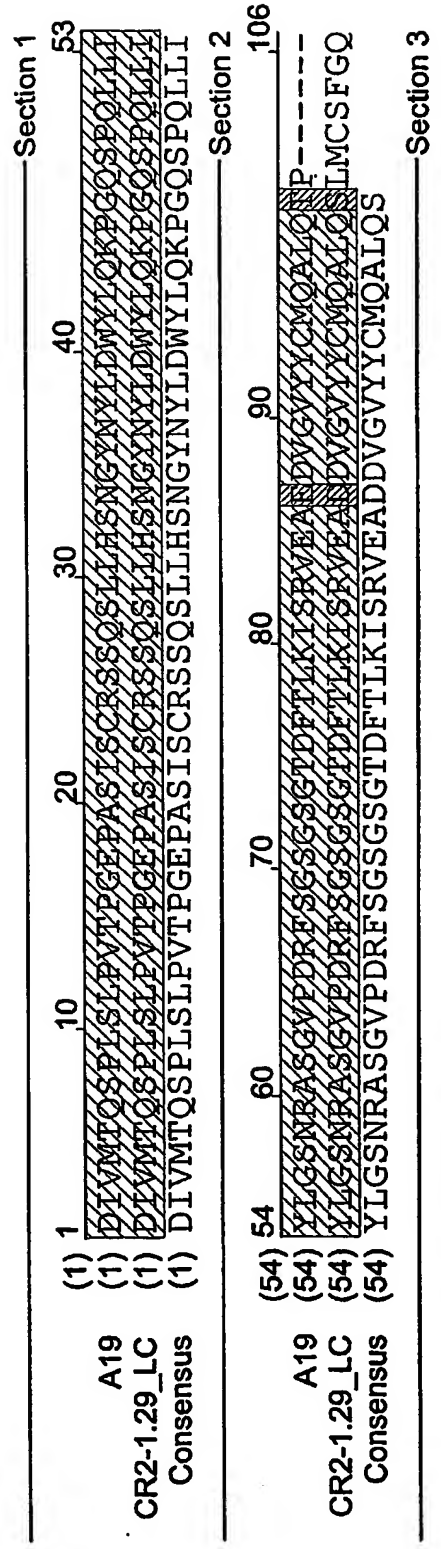

Section 1
Section 2
Section 3
A19
CR2-1.29_LC
Consensus
DIVMTQSPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQLLI
YLGSNRASGVPDRFSGSGSGTDFTLKISRVEADDVGVYYCMQALQ
P-------
LMCSFGQ
GTKLEIK

FIG. 31B

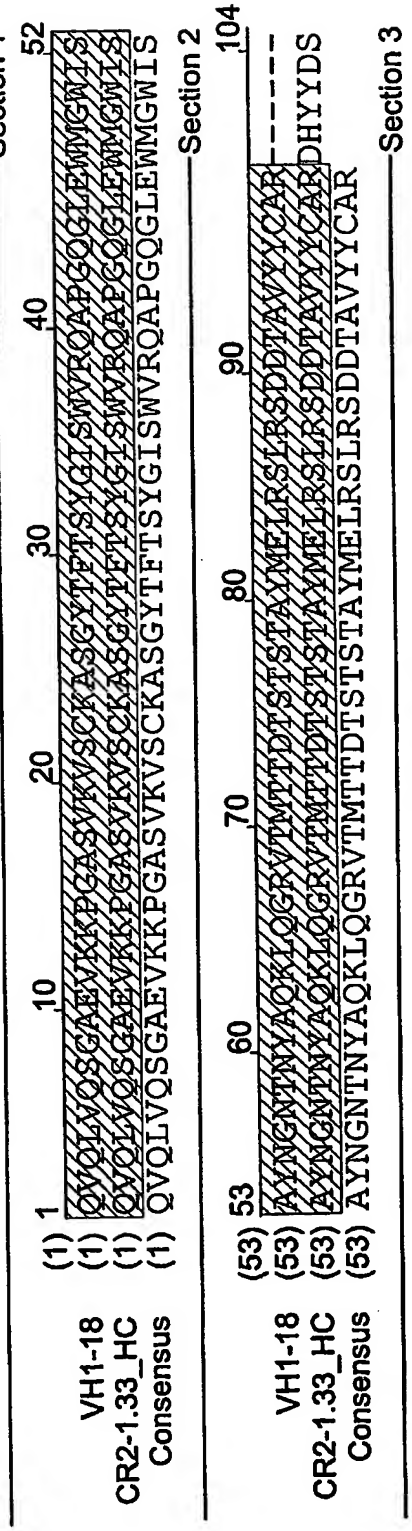

Section 1
Section 2
Section 3
VH1-18
CR2-1.33_HC
Consensus
QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYGISWVRQAPGQGLEWMGWIS
AYNGNTNYAQKLQGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCAR
SDYLYYYGLDVWGQGTTVTVSS

FIG. 32A

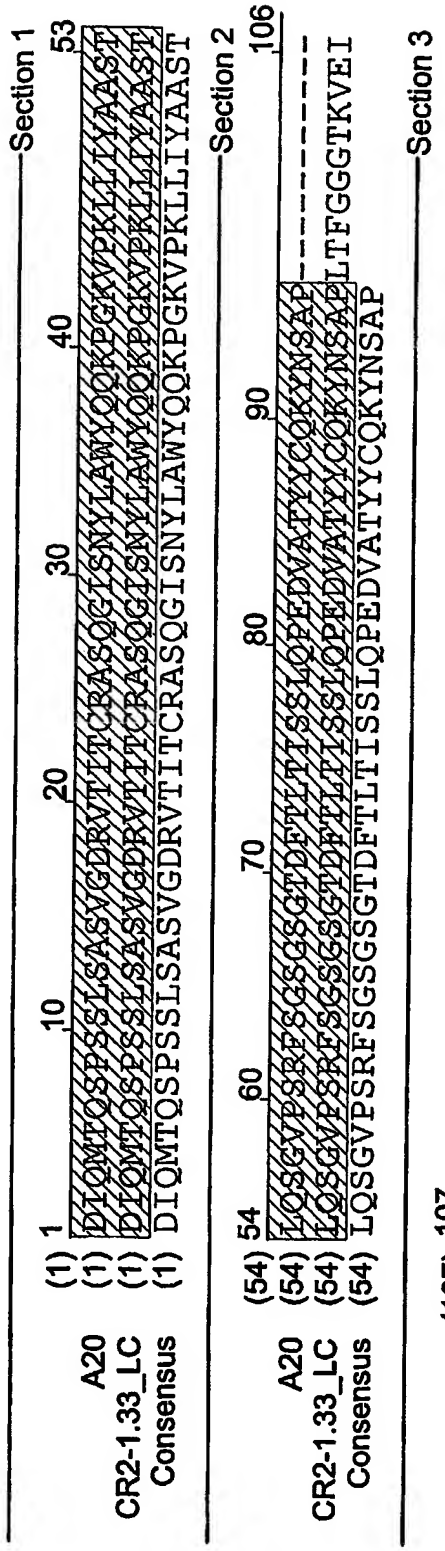

Section 1
Section 2
Section 3
A20
CR2-1.33_LC
Consensus
DIQMTQSPSSLSASVGDRVTITCRASQGISNYLAWYQQKPGKVPKLLIYAAST
LQSGVPSRFSGSGSGTDFTLTISSLQPEDVATYYCQKYNSAP
LTFGGGTKVEI
K

FIG. 32B

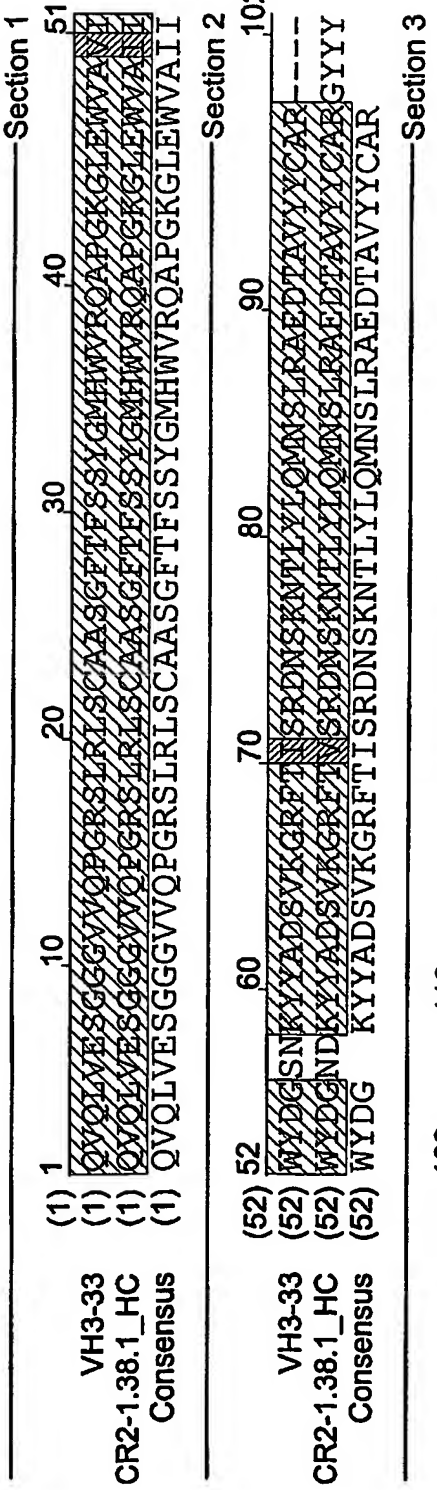

Section 1
Section 2
Section 3
VH3-33
CR2-1.38.1_HC
Consensus
QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAII
WYDGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR
DSSDYLYYYGMDVWGQGTTVTVSS

FIG. 33A

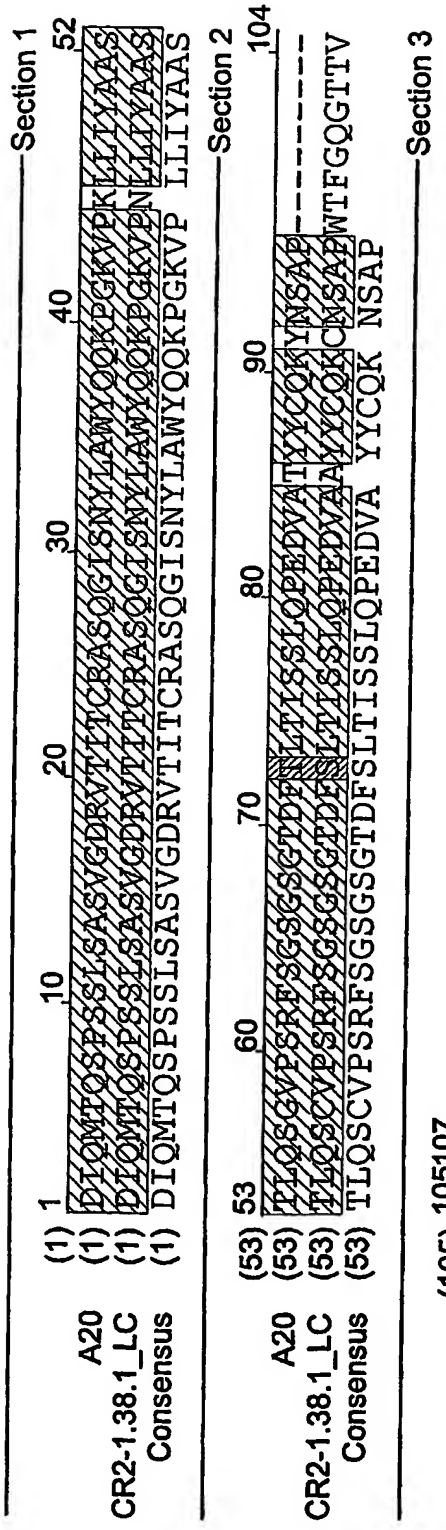

Section 1
Section 2
Section 3
A20
CR2-1.38.1_LC
Consensus
(1) 1 10 20 30 40 52
(1) DIQMTQSPSSLSASVGDRVTITCRASQGISNYLAWYQQKPGKVPKLLIYAAS
(1) DIQMTQSPSSLSASVGDRVTITCRASQGISNYLAWYQQKPGKVPNLLIYAAS
(1) DIQMTQSPSSLSASVGDRVTITCRASQGISNYLAWYQQKPGKVP LLIYAAS
(53) 53 60 70 80 90 104
(53) TLQSGVPSRFSGSGSGTDFTLTISSLQPEDVATYYCQKYNSAP----------
(53) TLQSCVPSRFSGSGSGTDFTLTISSLQPEDVAAYYCQKCMSAPWTFGQGTTV
(53) TLQSCVPSRFSGSGSGTDFSLTISSLQPEDVA YYCQK NSAP
(105) 105 107
(96) ---
(105) EIK
(105)

FIG. 33B

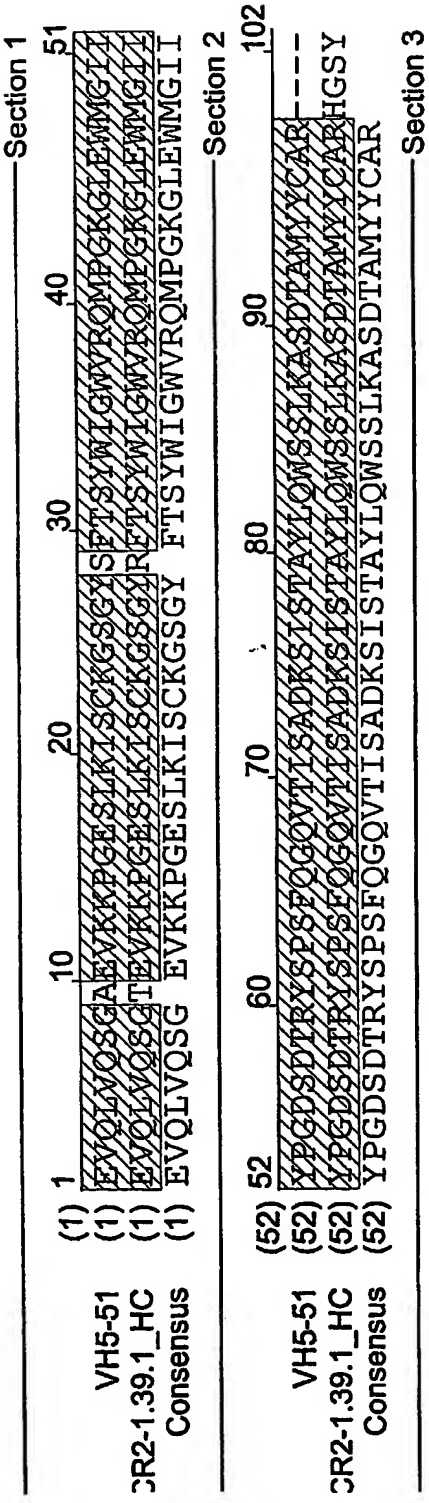

Section 1
Section 2
Section 3
VH5-51
CR2-1.39.1_HC
Consensus
EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGII
YPGDSDTRYSPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCAR
YYNSGSYYNVFDYWGQGTLVTVSS

FIG. 34A

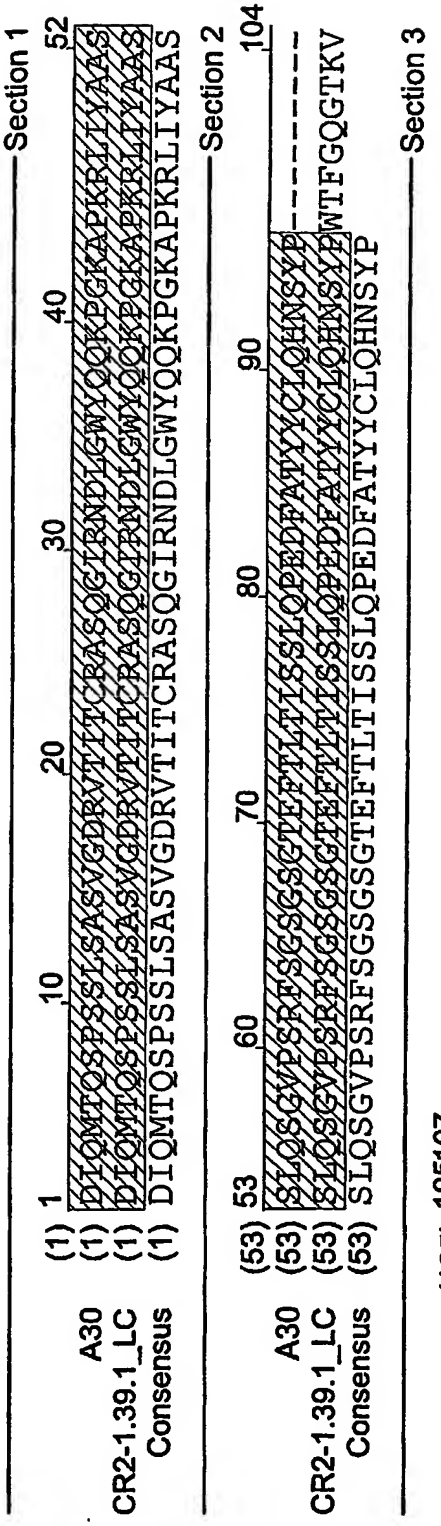

Section 1
10
20
30
40
(1) 1
A30 (1)
CR2-1.39.1_LC (1)
Consensus (1)
DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPGKAPKRLIYAAS
Section 2
60
70
80
90
(53) 53
A30 (53)
CR2-1.39.1_LC (53)
Consensus (53)
SLQSGVPSRFSGSGSGTEFTLTISSLQPEDFATYYCLQHNSYP
Section 3
(105) 105107
A30 (96) ---
CR2-1.39.1_LC (105) EIK
Consensus (105)

FIG. 34B

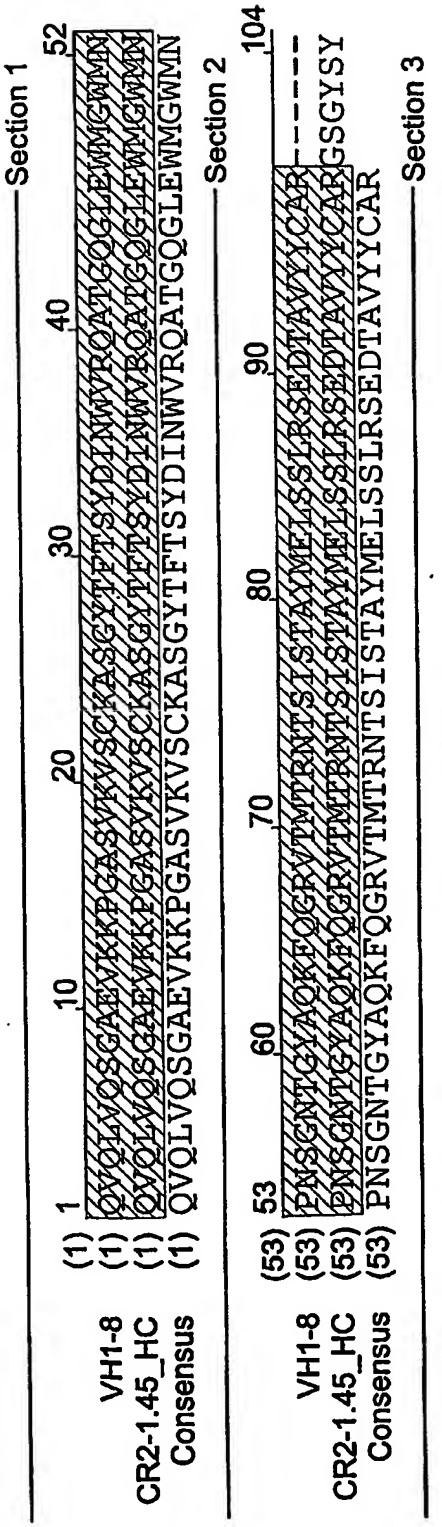

Section 1
Section 2
Section 3
VH1-8
CR2-1.45_HC
Consensus
QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDINWVRQATGQGLEWMGWMN
PNSGNTGYAQKFQGRVTMTRNTSISTAYMELSSLRSEDTAVYYCAR
GYDYYYGMDVWGQGTTVTVSS

FIG. 35A

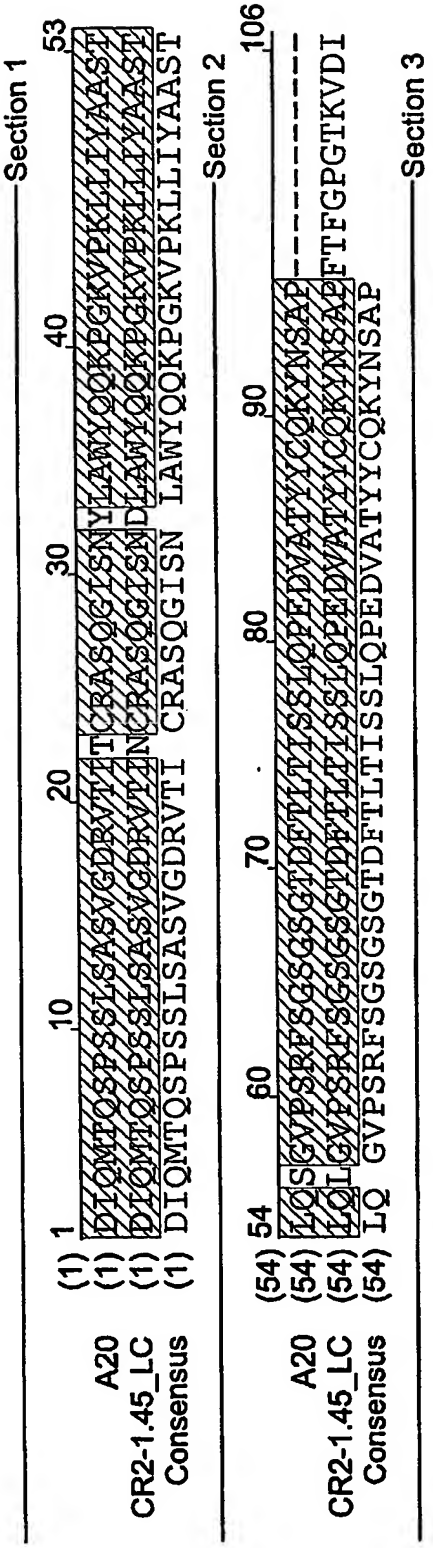

Section 1
Section 2
Section 3
A20
CR2-1.45_LC
Consensus
DIQMTQSPSSLSASVGDRVTITCRASQGISNYLAWYQQKPGKVPKLLIYAAST
LQGVPSRFSGSGSGTDFTLTISSLQPEDVATYYCQKYNSAPFTFGPGTKVDI
LQ GVPSRFSGSGSGTDFTLTISSLQPEDVATYYCQKYNSAP
(1) 1 10 20 30 40 53
(54) 54 60 70 80 90 106
(107) 107
(96) -
(107) K

FIG. 35B

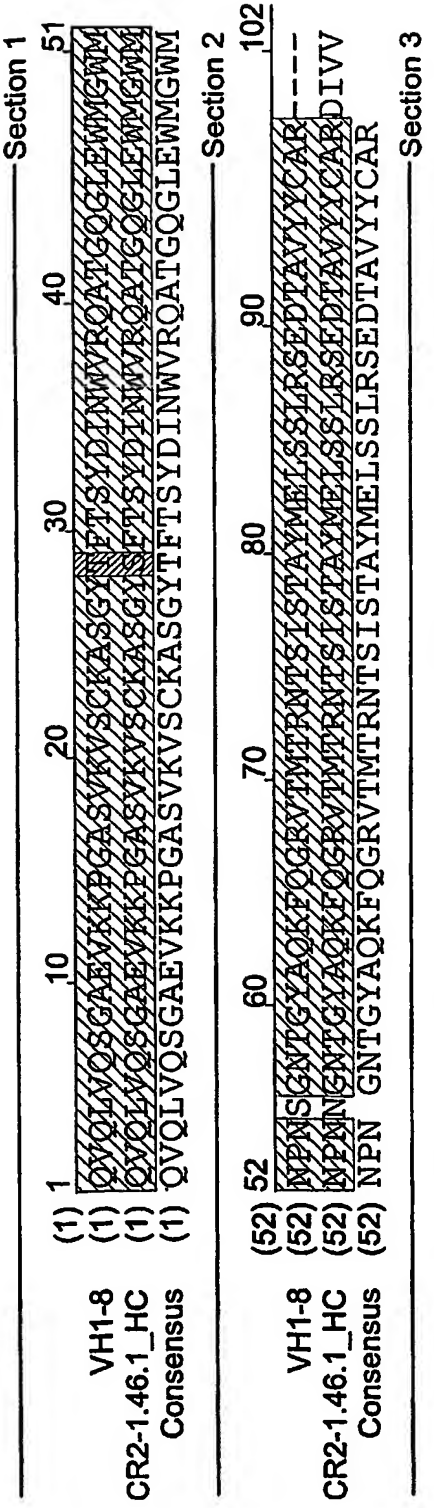

Section 1
Section 2
Section 3
VH1-8
CR2-1.46.1_HC
Consensus
QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDINWVRQATGQGLEWMGWM
NPNSGNTGYAQKFQGRVTMTRNTSISTAYMELSSLRSEDTAVYYCAR
VVTATDYYYGMDVWGQGTTVTVSS

FIG. 36A

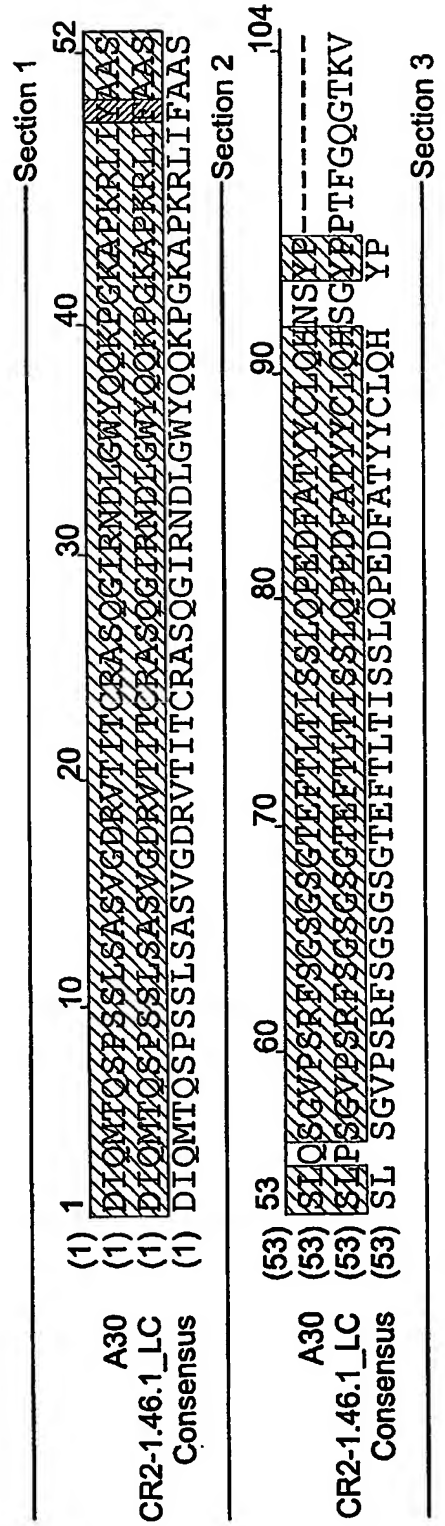

Section 1
Section 2
Section 3
A30
CR2-1.46.1_LC
Consensus
(1) DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPGKAPKRLIFAAS
(53) SLSGVPSRFSGSGSGTEFTLTISSLQPEDFATYYCLQHNSYPPTFGQGTKV
(105) EIK

FIG. 36B

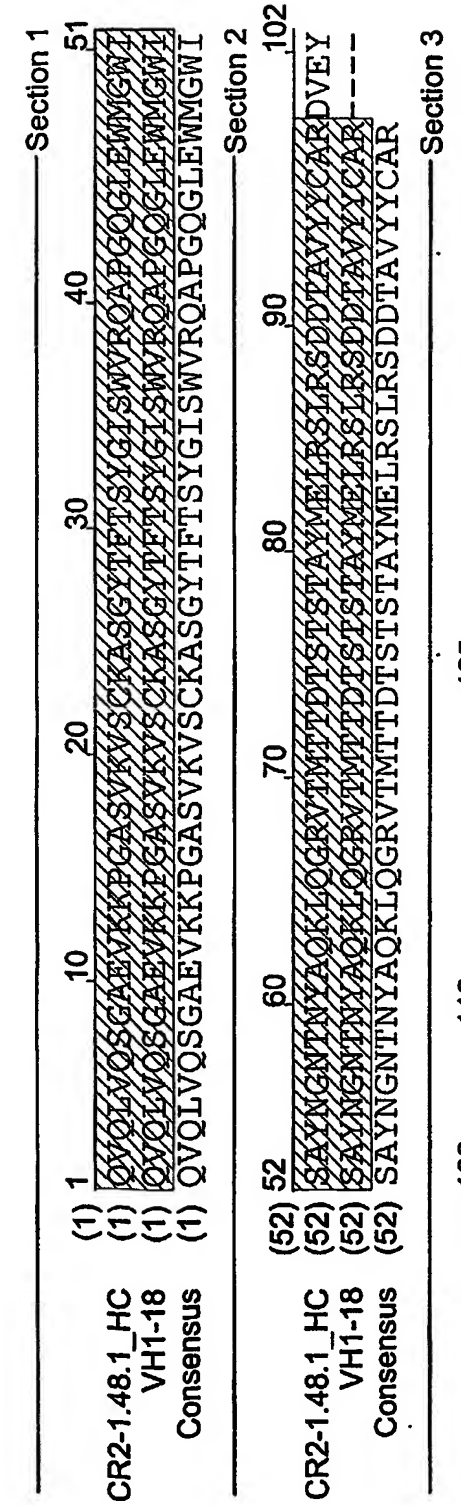

Section 1
Section 2
Section 3
CR2-1.48.1_HC
VH1-18
Consensus
QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYGISWVRQAPGQGLEWMGWI
YYDGSGYYYFDYWGQGTLVTVSS

FIG. 37A

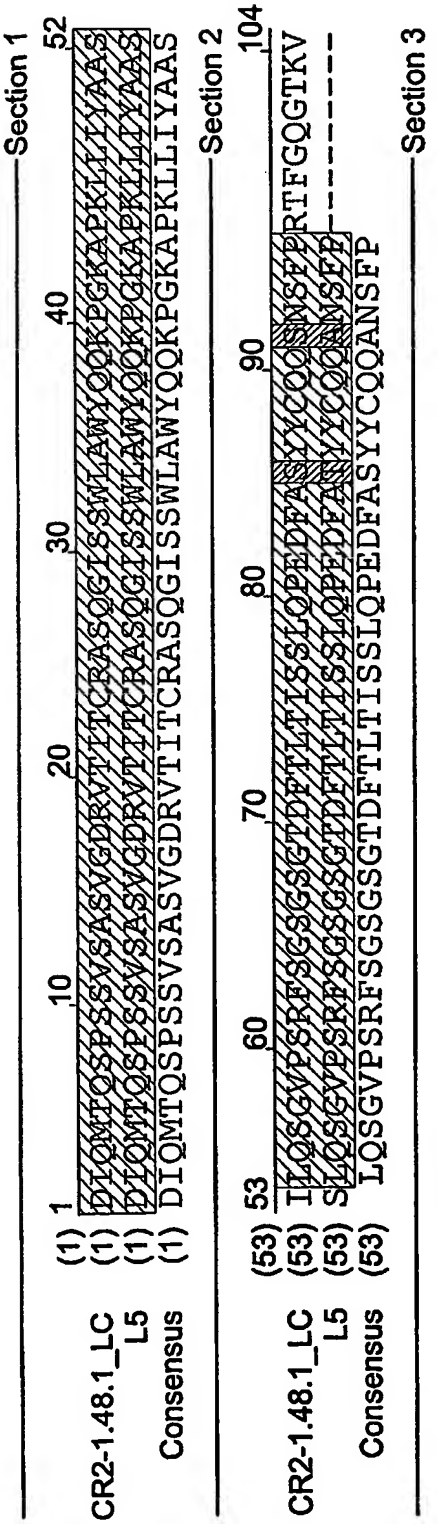

Section 1
Section 2
Section 3
CR2-1.48.1_LC
L5
Consensus
DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIYAAS
RTFGQGTKV
EIK-

FIG. 37B

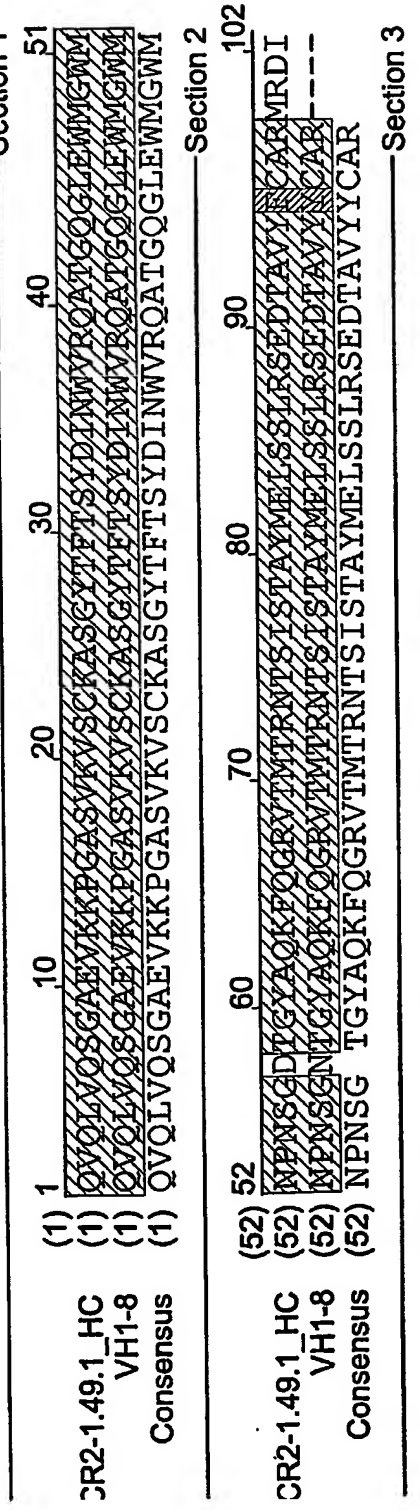

Section 1
Section 2
Section 3
CR2-1.49.1_HC
VH1-8
Consensus
QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDINWVRQATGQGLEWMGWM
NPNSGDTGYAQKFQGRVTMTRNTSISTAYMELSSLRSEDTAVYYCAR
VATSYYYYFYGMDVWGQGTTVTVSS

FIG. 38A

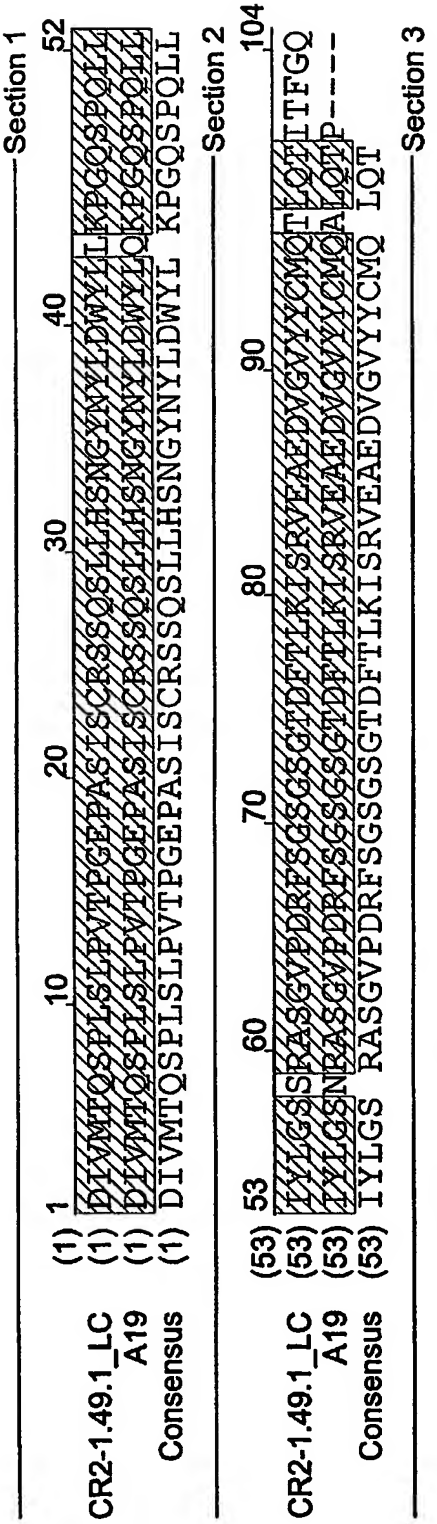

Section 1
Section 2
Section 3
CR2-1.49.1_LC
A19
Consensus
DIVMTQSPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLLKPGQSPQLL
IYLGSRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQTLQTFGQ
IYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTP----
IYLGS RASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQ LQT
GTRLEIK

FIG. 38B

Section 1
Section 2
Section 3
CR2-1.51.1_HC
VH5-51
Consensus
EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGII
EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGII
EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMGII
YPGDSDTRYSPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCAR
YPGDSDTRYSPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCAR
YPGDSDTRYSPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCAR
VWRNYRYTGWFDPWGQGTLVTVSS

FIG. 39A

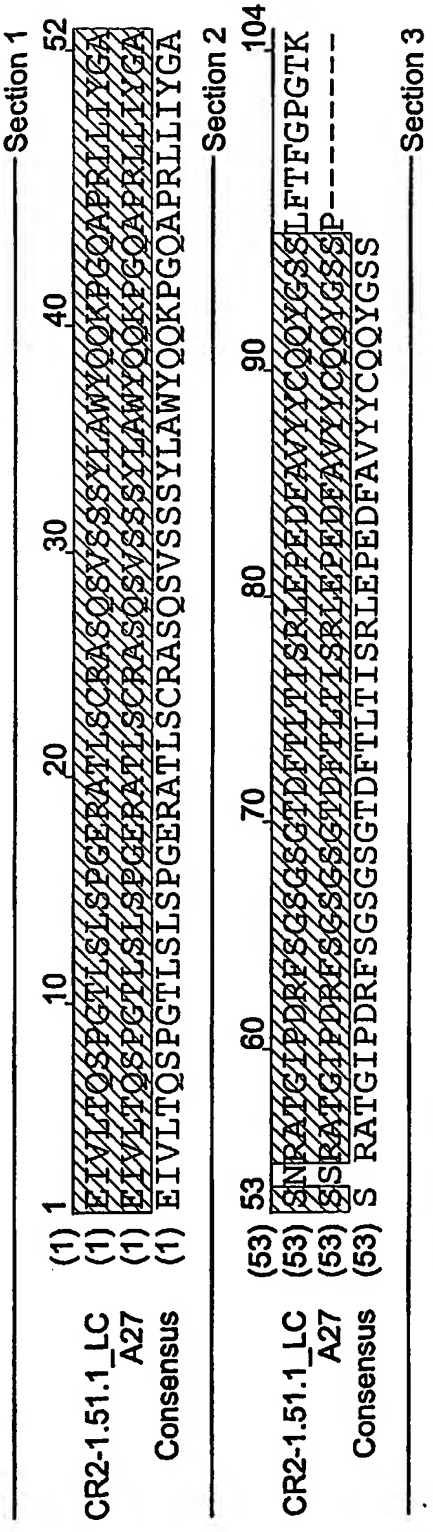

Section 1
Section 2
Section 3
CR2-1.51.1_LC
A27
Consensus
EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGA
EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGA
EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGA
S RATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSLFTFGPGTK
SRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSP--------
SRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSP--------
VDIK

FIG. 39B

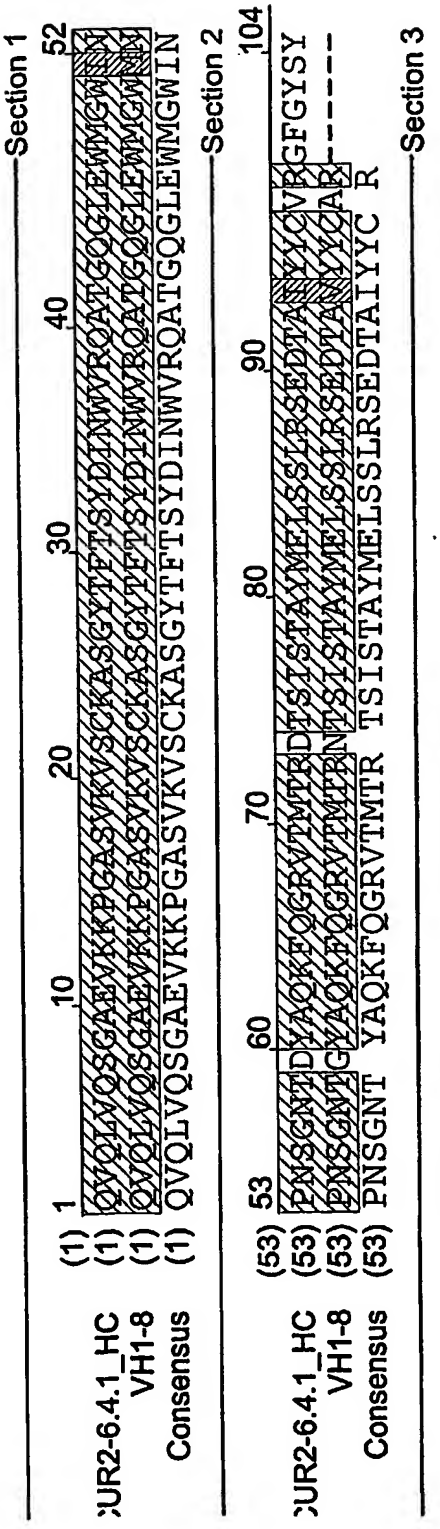

Section 1
Section 2
Section 3
CUR2-6.4.1_HC
VH1-8
Consensus
VH31-8
(1) QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDINWVRQATGQGLEWMGWIN
(53) PNSGNTDYAQKFQGRVTMTRDTSISTAYMELSSLRSEDTAVYYCVRGFGYSY
(105) NYDYYYGMDVWGQGTTVTVSS
(99) ----------

FIG. 40A

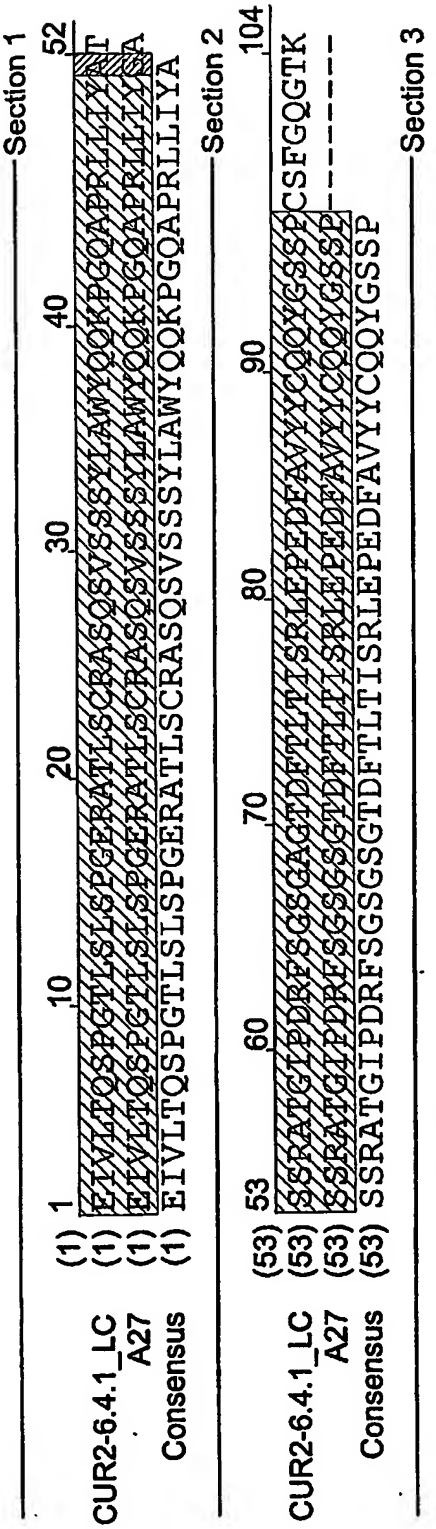

Section 1
Section 2
Section 3
CUR2-6.4.1_LC
A27
Consensus
EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYA
CSFGQGTK
LEIK

FIG. 40B

CLONE #	VH	# DEL	VH END	# N's	N Sequence	DH	Size of D	D Sequence	# N's	N Sequence	JH	# del	JH Segment
1.19.1	DP-15/1-8	-1	CGAGAG (SEQ ID NO:92)	3	ACG	D3-16	28	TTATGATTACGTTTG GGGGAGTTATCGT (SEQ ID NO:93)	2	GC	JH6B	-12	ACTACG (SEQ ID NO:94)
1.19.2	DP-15/1-8	-1	CGAGAG (SEQ ID NO:92)	3	ACG	D3-16	28	TTATGATTACGTTTG GGGGAGTTATCGT (SEQ ID NO:93)	2	GC	JH6B	-12	ACTACG (SEQ ID NO:94)
1.19.3	DP-15/1-8	-1	CGAGAG (SEQ ID NO:92)	3	ACG	D3-16	28	TTATGATTACGTTTG GGGGAGTTATCGT (SEQ ID NO:93)	2	GC	JH6B	-12	ACTACG (SEQ ID NO:94)
6.4.1	DP-15/1-8	0	GAGAGG (SEQ ID NO:95)	3	CTT	D5-18	12	TGGATACAGCTA (SEQ ID NO:96)	2	TA	JH6B	0	ATTACTAC (SEQ ID NO:97)
6.4.2	DP-15/1-8	0	GAGAGG (SEQ ID NO:95)	3	CTT	D5-18	12	TGGATACAGCTA (SEQ ID NO:96)	2	TA	JH6B	0	ATTACTAC (SEQ ID NO:97)
6.4.3	DP-15/1-8	0	GAGAGG (SEQ ID NO:95)	3	CTT	D5-18	12	TGGATACAGCTA (SEQ ID NO:96)	2	TA	JH6B	0	ATTACTAC (SEQ ID NO:97)

FIG. 41A

CLONE #	Vk	#del	Vk end	#n	N SEQ	Jk	# del	Jk end
1.19.1	A30	-3	TTACCC (SEQ ID NO:98)	6	GTGCAG (SEQ ID NO:99)	JK2	-7	TTTTGG (SEQ ID NO:100)
1.19.2	A30	-3	TTACCC (SEQ ID NO:98)	6	GTGCAG (SEQ ID NO:99)	JK2	-7	TTTTGG (SEQ ID NO:100)
1.19.3	A30	-3	TTACCC (SEQ ID NO:98)	6	GTGCAG (SEQ ID NO:99)	JK2	-7	TTTTGG (SEQ ID NO:100)
6.4.1	A27/A27A	-3	CTCACC (SEQ ID NO:101)	6	GTGCAG (SEQ ID NO:102)	JK2	-7	TTTTGG (SEQ ID NO:103)
6.4.2	A27/A27A	-3	CTCACC (SEQ ID NO:101)	6	GTGCAG (SEQ ID NO:102)	JK2	-7	TTTTGG (SEQ ID NO:103)
6.4.3	A27/A27A	-3	CTCACC (SEQ ID NO:101)	6	GTGCAG (SEQ ID NO:102)	JK2	-7	TTTTGG (SEQ ID NO:103)

FIG. 41B

CLONE #	VH	#DEL	VH END	# N's	N Sequence	DH	Size of D	D Sequence	# N's	N Sequence	JH	# del	JH Segment
1.6.1	DP-77/3-21	0	GAGAGA (SEQ ID NO:104)	0	0	D3-16	22	TATTATGATTAC GTTTGGGGGA (SEQ ID NO:105)	14	ATTATCGCC TCGTT (SEQ ID NO:106)	JH4 B	-1	CTACTT (SEQ ID NO:107)
1.6.1	DP-77/3-21	0	GAGAGA (SEQ ID NO:104)	0	0	D3-16	22	TATTATGATTAC GTTTGGGGGA (SEQ ID NO:105)	14	ATTATCGCC TCGTT (SEQ ID NO:106)	JH4 B	-1	CTACTT (SEQ ID NO:107)
1.6.1	DP-77/3-21	0	GAGAGA (SEQ ID NO:104)	0	0	D3-16	22	TATTATGATTAC GTTTGGGGGA (SEQ ID NO:105)	14	ATTATCGCC TCGTT (SEQ ID NO:106)	JH4 B	-1	CTACTT (SEQ ID NO:107)
1.11.1	DP-42/3-53	-5	AGAGA (SEQ ID NO:108)	3	GGA	D4-17	10	ACGGTGACTA (SEQ ID NO:109)	5	CGAAT (SEQ ID NO:110)	JH6 B	-2	TACTACTA (SEQ ID NO:111)
1.11.2	DP-42/3-53	-5	AGAGA (SEQ ID NO:108)	3	GGA	D4-17	10	ACGGTGACTA (SEQ ID NO:109)	5	CGAAT (SEQ ID NO:110)	JH6 B	-2	TACTACTA (SEQ ID NO:111)
1.23.1	DP-73/5-51	0	GAGACA (SEQ ID NO:112)	18	TGTATCGTATTACT ATGT (SEQ ID NO:113)	D3-10	19	TTCGGGGAGTTA TTATAAC (SEQ ID NO:114)	2	GT	JH4 B	-4	CTTTGA (SEQ ID NO:115)
1.23.2	DP-73/5-51	0	GAGACA (SEQ ID NO:112)	18	TGTATCGTATTACT ATGT (SEQ ID NO:113)	D3-10	19	TTCGGGGAGTTA TTATAAC (SEQ ID NO:114)	2	GT	JH4 B	-4	CTTTGA (SEQ ID NO:115)

FIG. 42A

CLONE #	Vk	#del	vk end	#n	N SEQ	Jk	# del	JK end
1.6.1	A30	-3	TTACCC (SEQ ID NO:116)	0	0	JK4	0	GCTCACT (SEQ ID NO:117)
1.6.2	A30	-3	TTACCC (SEQ ID NO:116)	0	0	JK4	0	GCTCACT (SEQ ID NO:117)
1.6.3	A30	-3	TTACCC (SEQ ID NO:116)	0	0	JK4	0	GCTCACT (SEQ ID NO:117)
1.11.1	A3/A19/DPK	-4	AAACTC (SEQ ID NO:118)	0	0	JK4	-2	TCACTTTC (SEQ ID NO:119)
1.11.2	A3/A19/DPK	-4	AAACTC (SEQ ID NO:118)	0	0	JK4	-2	TCACTTTC (SEQ ID NO:119)
1.23.1	A30	-3	TTACCC (SEQ ID NO:120)	0	0	JK1	0	GTGGAC (SEQ ID NO:120)
1.23.2	A30	-3	TTACCC (SEQ ID NO:120)	0	0	JK1	0	GTGGAC (SEQ ID NO:120)

FIG. 42B

CLONE #	VH	#DEL	VH END	# N's	N Sequence	DH	Size of D	D Sequence	# N's	N Sequence	JH	# del	JH Segment
1.17.1	DP-50/3-33	0	GAGAGA (SEQ ID NO:121)	4	TCAA	D5-18	8	GGATACA (SEQ ID NO:122)	9	ATATGCTG G (SEQ ID NO:123)	JH6B	-1	TTACTACT (SEQ ID NO:124)
1.17.2	DP-50/3-33	0	GAGAGA (SEQ ID NO:121)	4	TCAA	D5-18	8	GGATACA (SEQ ID NO:122)	9	ATATGCTG G (SEQ ID NO:123)	JH6B	-1	TTACTACT (SEQ ID NO:124)
1.17.3	DP-50/3-33	0	GAGAGA (SEQ ID NO:121)	4	TCAA	D5-18	8	GGATACA (SEQ ID NO:122)	9	ATATGCTG G (SEQ ID NO:123)	JH6B	-1	TTACTACT (SEQ ID NO:124)
1.18	DP-15/1-8	1	CGAGAG (SEQ ID NO:125)	1	A	D6-19	19	GGGTATAGCAGT GGCTGG (SEQ ID NO:126)	4	GACA	JH6B	-2	TACTAC (SEQ ID NO:127)
1.24.1	DP-50/3-33	0	GAGAGA (SEQ ID NO:128)	4	TCAG	DK4	18	GGATACAGCTAT GGTTAC (SEQ ID NO:129)	2	GT	JH6B	-4	CTACTA (SEQ ID NO:130)
1.24.2	DP-50/3-33	0	GAGAGA (SEQ ID NO:128)	4	TCAG	DK4	18	GGATACAGCTAT GGTTAC (SEQ ID NO:129)	2	GT	JH6B	-4	CTACTA (SEQ ID NO:130)
1.25.1	DP-73/5-51	0	GAGACA (SEQ ID NO:131)	6	TGGATC (SEQ ID NO:132)	D3-10	30	GTAtTATTATGG TTCGGAGAcTTA TTATAA (SEQ ID NO:133)	3	TGT	JH4B	-4	CTTTGA (SEQ ID NO:135)

FIG. 43A

SUBSTITUTE SHEET (RULE 26)

CLONE #	VH	#DEL	VH END	# N's	N Sequence	DH	Size of D	D Sequence	# N's	N Sequence	JH	# del	JH Segment
1.25.2	DP-73/5-51	0	GAGACA (SEQ ID NO:131)	6	TGGATC (SEQ ID NO:132)	D3-10	30	GTACTATTATGG TTCGGAGACTTA TTATAA (SEQ ID NO:133)	3	TGT	JH4B	-4	CTTTGA (SEQ ID NO:134)
1.29	DP-73/5-51	0	GAGACA (SEQ ID NO:135)	1	C	D5-12	21	GTGGATGTAGGG GCTACGATT (SEQ ID NO:136)	7	GGGGAT (SEQ ID NO:137)	JH6B	0	ATTACTAC (SEQ ID NO:138)
1.33	DP-14/1-18	0	GAGAGA (SEQ ID NO:139)	2	TC	D21-9	18	ATTACTATGATA GTAGTG (SEQ ID NO:140)	7	ATTATCT (SEQ ID NO:141)	JH6B	-4	CTACTA (SEQ ID NO:142)
1.38.1	DP-50/3-33	1	CCAGAG (SEQ ID NO:143)	2	GA	D21-9	19	TATTACTATGAT AGTAGTG (SEQ ID NO:144)	7	ATTATCT (SEQ ID NO:145)	JH6B	-4	CTACTA (SEQ ID NO:146)
1.39.1	DP-73/5-51	0	GAGACA (SEQ ID NO:147)	6	TGGATC (SEQ ID NO:148)	D3-10	31	GTATTACTATaa TTCGGGAGTTA TTATAAC (SEQ ID NO:149)	2	GT	JH4B	-4	CTTTGA (SEQ ID NO:150)
1.39.2	DP-73/5-51	0	GAGACA (SEQ ID NO:147)	6	TGGATC (SEQ ID NO:148)	D3-10	31	GTATTACTATaa TTCGGGAGTTA TTATAAC (SEQ ID NO:149)	2	GT	JH4B	-4	CTTTGA (SEQ ID NO:150)

FIG. 43B

CLONE #	VH	#DEL	VH END	# N's	N Sequence	DH	Size of D	D Sequence	# N's	N Sequence	JH	# del	JH Segment
1.40.1	DP-15/1-8	1	CGAGAG (SEQ ID NO:151)	0	0	D2	25	ATATTGTAGTGG TGGTAGCTGCTA C (SEQ ID NO:152)	2	CA	JH6B	-6	ACTACT (SEQ ID NO:153)
1.40.2	DP-15/1-8	1	CGAGAG (SEQ ID NO:151)	0	0	D2	25	ATATTGTAGTGG TGGTAGCTGCTA C (SEQ ID NO:152)	2	CA	JH6B	-6	ACTACT (SEQ ID NO:153)
1.45	DP-15/1-8	0	GAGAGG (SEQ ID NO:154)	2	CA	DK4	20	GTGGATACAGCT ATGGTTAC (SEQ ID NO:155)	1	G	JH6B	-6	ACTACT (SEQ ID NO:156)
1.46.1	DP-15/1-8	1	CGAGAG (SEQ ID NO:157)	0	0	D2	25	ATATTGTAGT GGTGGTAGCTGC TAC (SEQ ID NO:158)	2	GG	JH6B	-6	ACTACT (SEQ ID NO:159)
1.46.2	DP-15/1-8	1	CGAGAG (SEQ ID NO:157)	0	0	D2	25	ATATTGTAGTGG TGGTAGCTGCTA C (SEQ ID NO:158)	2	GG	JH6B	-6	ACTACT (SEQ ID NO:159)
1.48.1	DP-14/1-18	1	CGAGAG (SEQ ID NO:160)	7	TGTTGAA (SEQ ID NO:161)	D21-9	20	TATTACTATGAT gGTAGTGGTTAT (SEQ ID NO:162)	1	T	JH4B	0	ACTACT (SEQ ID NO:163)

FIG. 43C

CLONE #	VH	#DEL	VH END	# N's	N Sequence	DH	Size of D	D Sequence	# N's	N Sequence	JH	# del	JH Segment
1.48.2	DP-14/1-18	1	CGAGAG (SEQ ID NO:160)	7	TGTTGAA (SEQ ID NO:161)	D21-9	20	TATTACTATGAT gGTAGTGGTTAT (SEQ ID NO:162)	1	T	JH4B	0	ACTACT (SEQ ID NO:163)
1.49.1	DP-15/1-8	2	GCGAGA (SEQ ID NO:164)	5	ATGAG (SEQ ID NO:165)	D5-12	17	GGATATAGTGGC TACGA (SEQ ID NO:166)	3	GCT	JH6B	0	ATTACTAC (SEQ ID NO:167)
1.49.2	DP-15/1-8	2	GCGAGA (SEQ ID NO:164)	5	ATGAG (SEQ ID NO:165)	D5-12	17	GGATATAGTGGC TACGA (SEQ ID NO:166)	3	GCT	JH6B	0	ATTACTAC (SEQ ID NO:167)
1.51.1	DP-73/5-51	0	GAGACA (SEQ ID NO:168)	1	C	D3-16	31	TATGATTACGTT TGGaGGAaTTAT CGGTATA (SEQ ID NO:169)	5	CAGGG (SEQ ID NO:170)	JH5B	-5	TGGTTC (SEQ ID NO:171)
1.51.2	DP-73/5-51	0	GAGACA (SEQ ID NO:168)	1	C	D3-16	31	TATGATTACGTT TGGaGGAaTTAT CGGTATA (SEQ ID NO:169)	5	CAGGG (SEQ ID NO:170)	JH5B	-5	TGGTTC (SEQ ID NO:171)

CLONE #	vk	#del	vk end	#n	N SEQ	Jk	# del	JK end
1.17.1	A30	3	TTACCC (SEQ ID NO:172)	0	0	JK4	0	GCTCACT (SEQ ID NO:173)
1.17.2	A30	3	TTACCC (SEQ ID NO:172)	0	0	JK4	0	GCTCACT (SEQ ID NO:173)

FIG. 43D

CLONE #	vk	#del	vk end	#n	N SEQ	Jk	# del	JK end
1.17.3	A30	3	TTACCC (SEQ ID NO:172)	0	0	JK4	0	GCTCACT (SEQ ID NO:173)
1.18	A30	3	TTACCC (SEQ ID NO:174)	0	0	JK3	0	ATTCAC (SEQ ID NO:175)
1.24.1	A30	3	TTACCC (SEQ ID NO:176)	0	0	JK1	0	GTGGAC (SEQ ID NO:177)
1.24.2	A30	3	TTACCC (SEQ ID NO:176)	0	0	JK1	0	GTGGAC (SEQ ID NO:177)
1.25.1	A30	3	TTACCC (SEQ ID NO:178)	0	0	JK1	0	GTGGAC (SEQ ID NO:179)
1.25.2	A30	3	TTACCC (SEQ ID NO:178)	0	0	JK1	0	GTGGAC (SEQ ID NO:179)
1.29	A3/A19/DPK	7	CTACAA (SEQ ID NO:180)	14	TCTCTCATG TGCAG (SEQ ID NO:181)	JK2	-7	TTTTGG (SEQ ID NO:182)
1.33	A20/DPK4	3	TGCCCC (SEQ ID NO:183)	0	0	JK4	0	GCTCAC (SEQ ID NO:184)
1.38.1	A20/DPK4	3	TGCCCC (SEQ ID NO:185)	0	0	JK1	0	GTGGAC (SEQ ID NO:186)
1.39.1	A30	3	TTACCC (SEQ ID NO:187)	0	0	JK1	0	GTGGAC (SEQ ID NO:188)

FIG. 43E

CLONE #	vk	#del	vk end	#n	N SEQ	Jk	# del	JK end
1.39.2	A30	3	TTACCC (SEQ ID NO:187)	0	0	JK1	0	GTGGAC (SEQ ID NO:188)
1.45	A20/DPK4	3	TGCCCC (SEQ ID NO:189)	0	0	JK3	0	ATTCAC (SEQ ID NO:190)
1.46.1	A30	0	CCCTCC (SEQ ID NO:191)	0	0	JK1	-3	GACGTT (SEQ ID NO:192)
1.46.2	A30	0	CCCTCC (SEQ ID NO:191)	0	0	JK1	-3	GACGTT (SEQ ID NO:192)
1.48.1	L5/DPK5/V	1	TCCCTC (SEQ ID NO:193)	0	0	JK1	-2	GGACGTT (SEQ ID NO:194)
1.48.2	L5/DPK5/V	1	TCCCTC (SEQ ID NO:193)	0	0	JK1	-2	GGACGTT (SEQ ID NO:194)
1.49.1	A3/A19/DPK	5	CAAACT (SEQ ID NO:195)	0	0	JK5	-1	ATCACC (SEQ ID NO:196)
1.49.2	A3/A19/DPK	5	CAAACT (SEQ ID NO:195)	0	0	JK5	-1	ATCACC (SEQ ID NO:196)
1.51.1	A27/A27A	4	GCTCAC (SEQ ID NO:197)	1	T	JK3	0	ATTCAC (SEQ ID NO:198)
1.51.1	A27/A27A	4	GCTCAC (SEQ ID NO:197)	1	T	JK3	0	ATTCAC (SEQ ID NO:198)

FIG. 43F

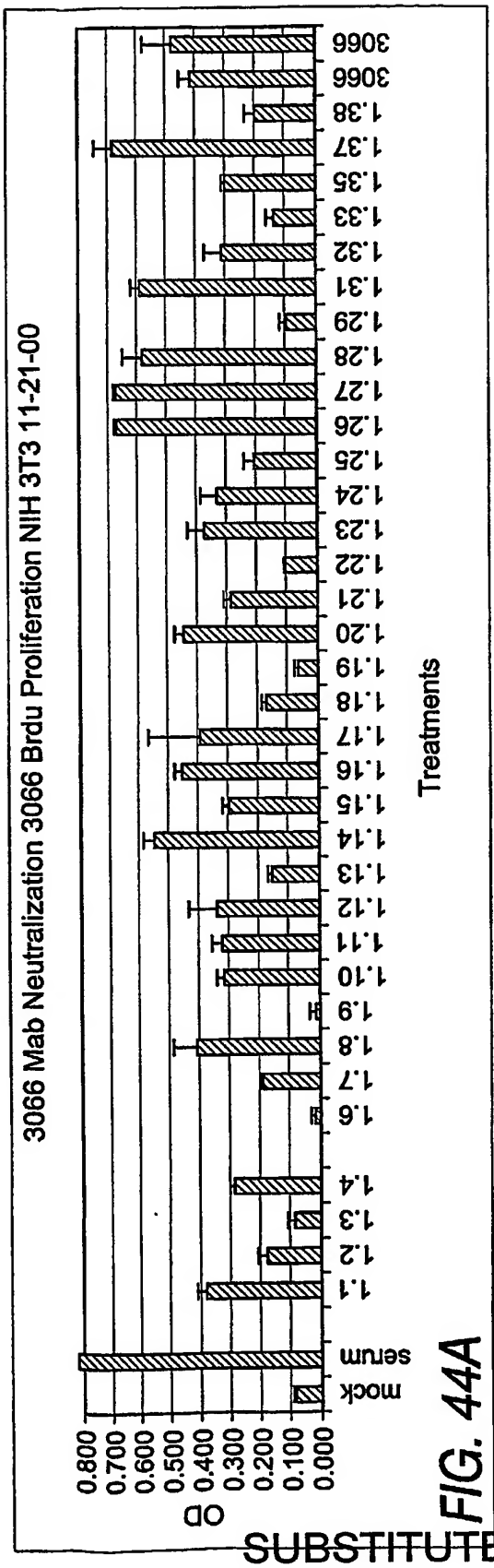


FIG. 44A

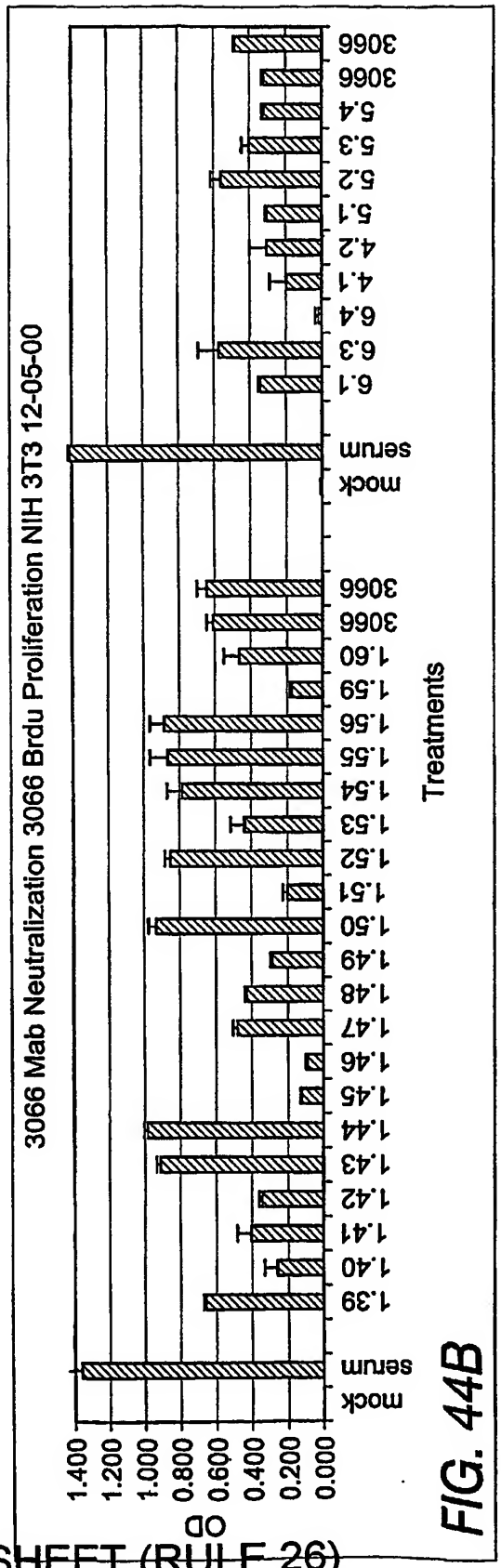


FIG. 44B

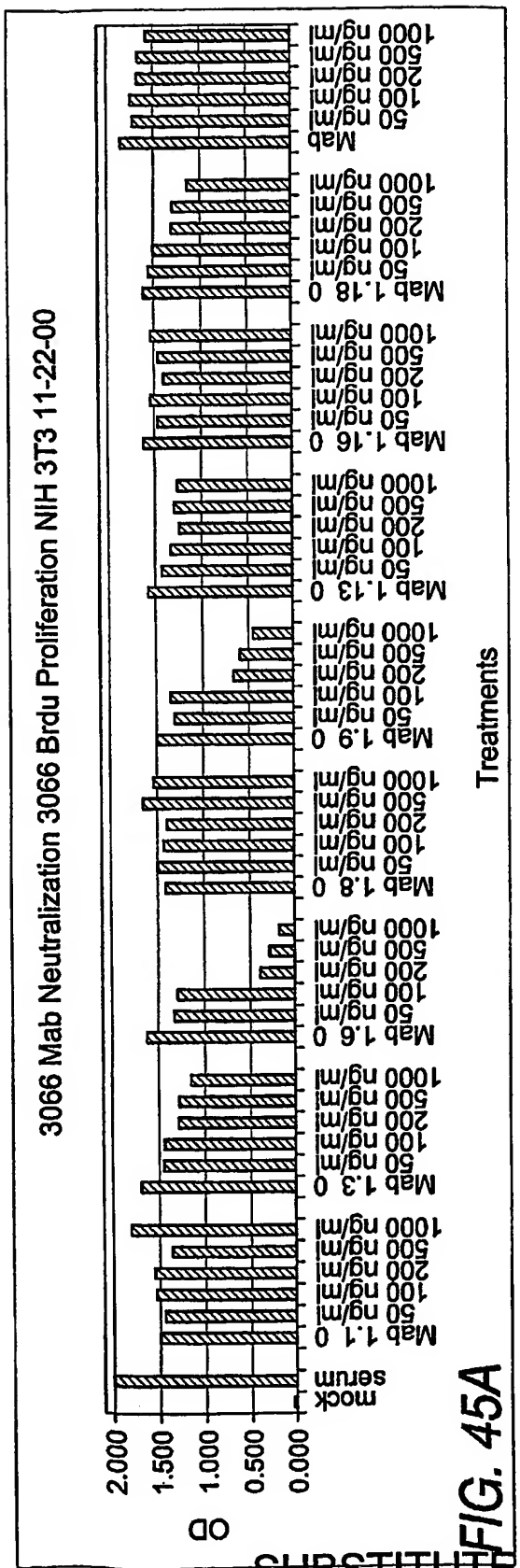


FIG. 45A

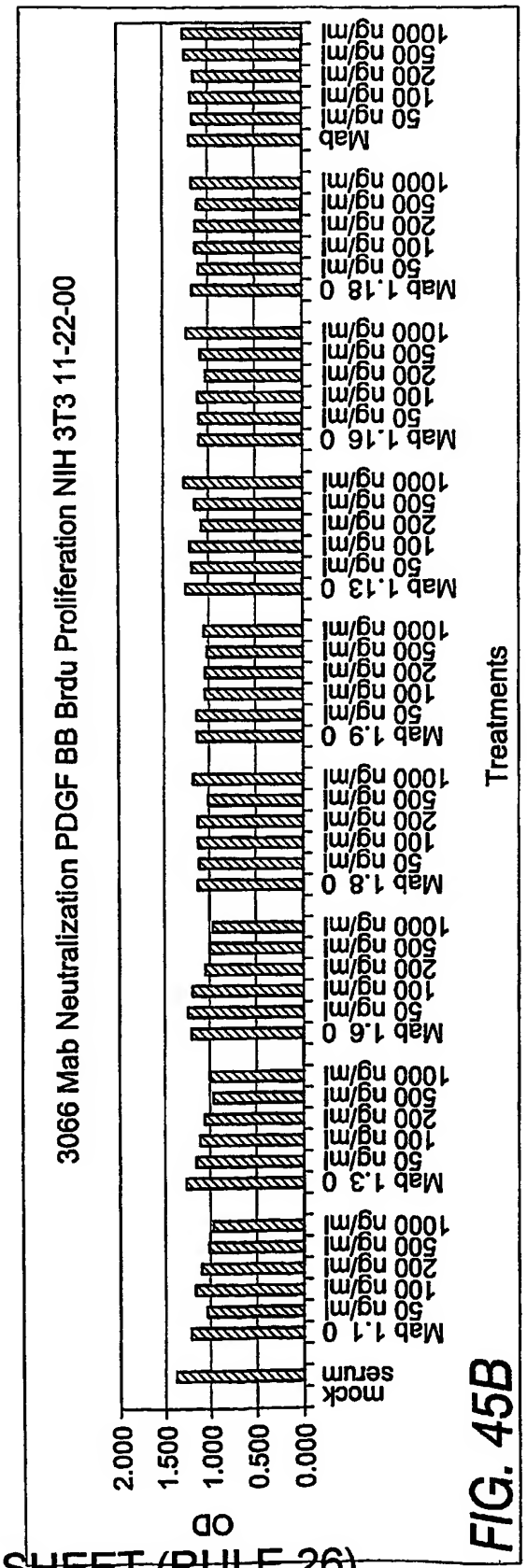


FIG. 45B

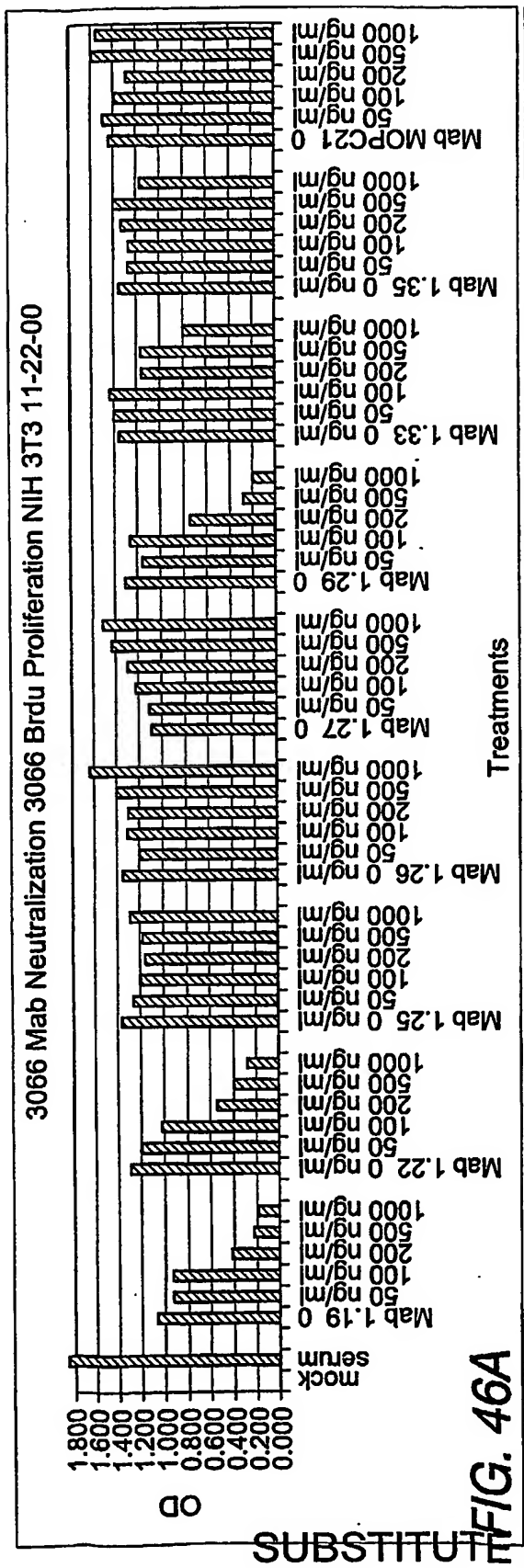


FIG. 46A

FIG. 46B

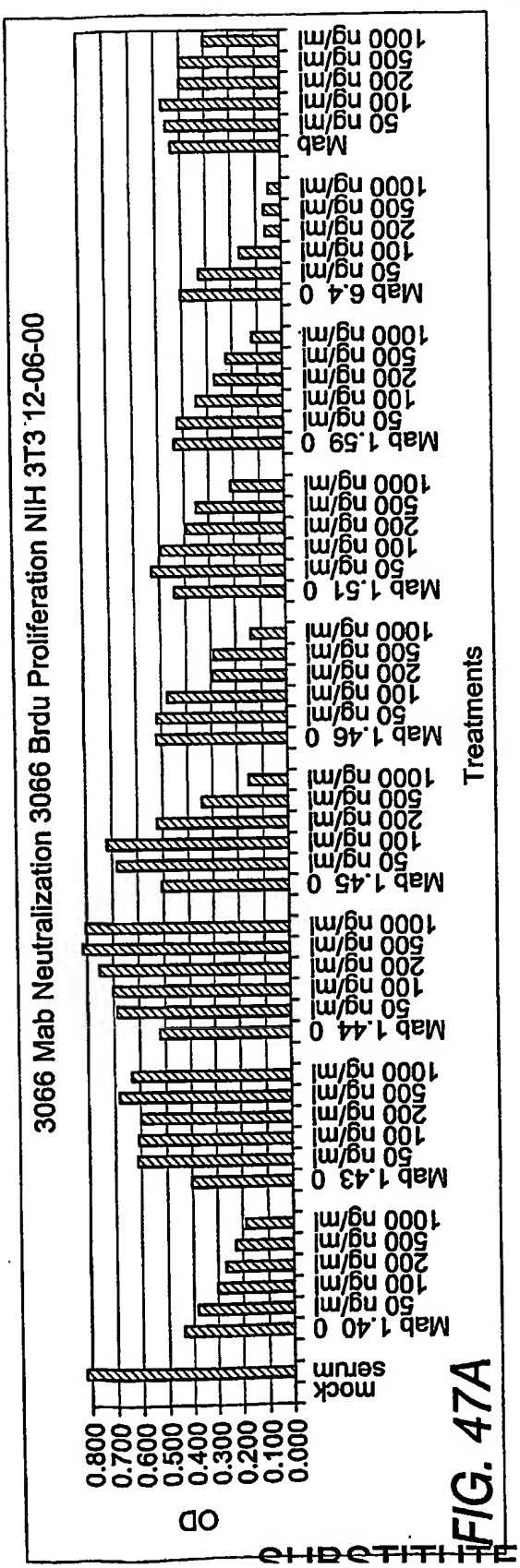


FIG. 47A

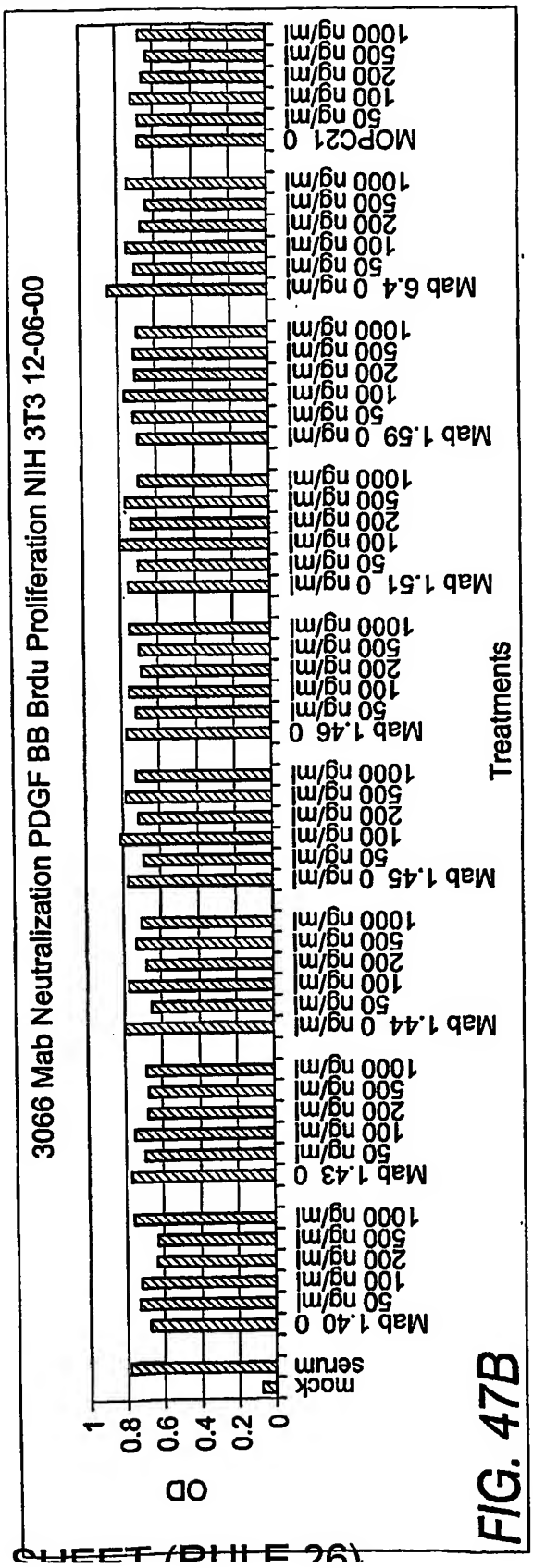
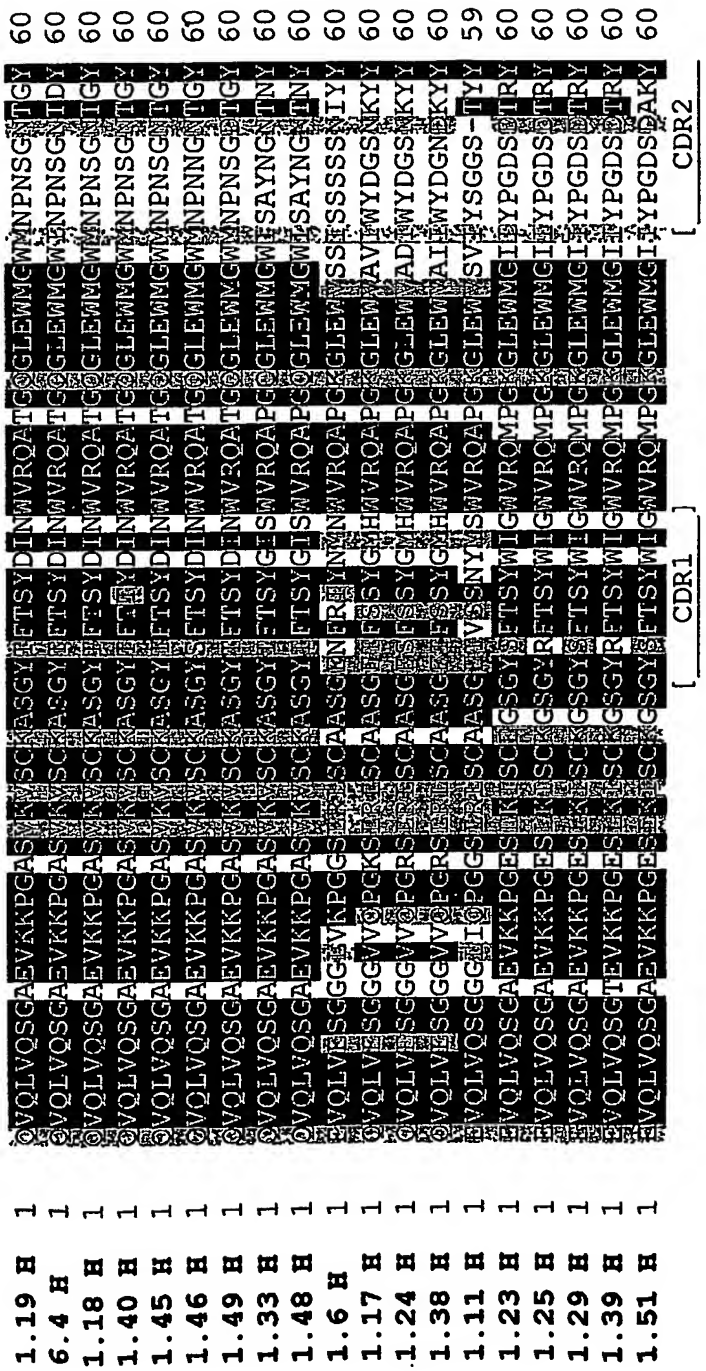


FIG. 47B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6.4 H
1.18 H
1.40 H
1.45 H
1.46 H
1.49 H
1.33 H
1.48 H
1.6 H
1.17 H
1.24 H
1.38 H
1.11 H
1.23 H
1.25 H
1.29 H
1.39 H
1.51 H
CDR1
CDR2

FIG. 48A

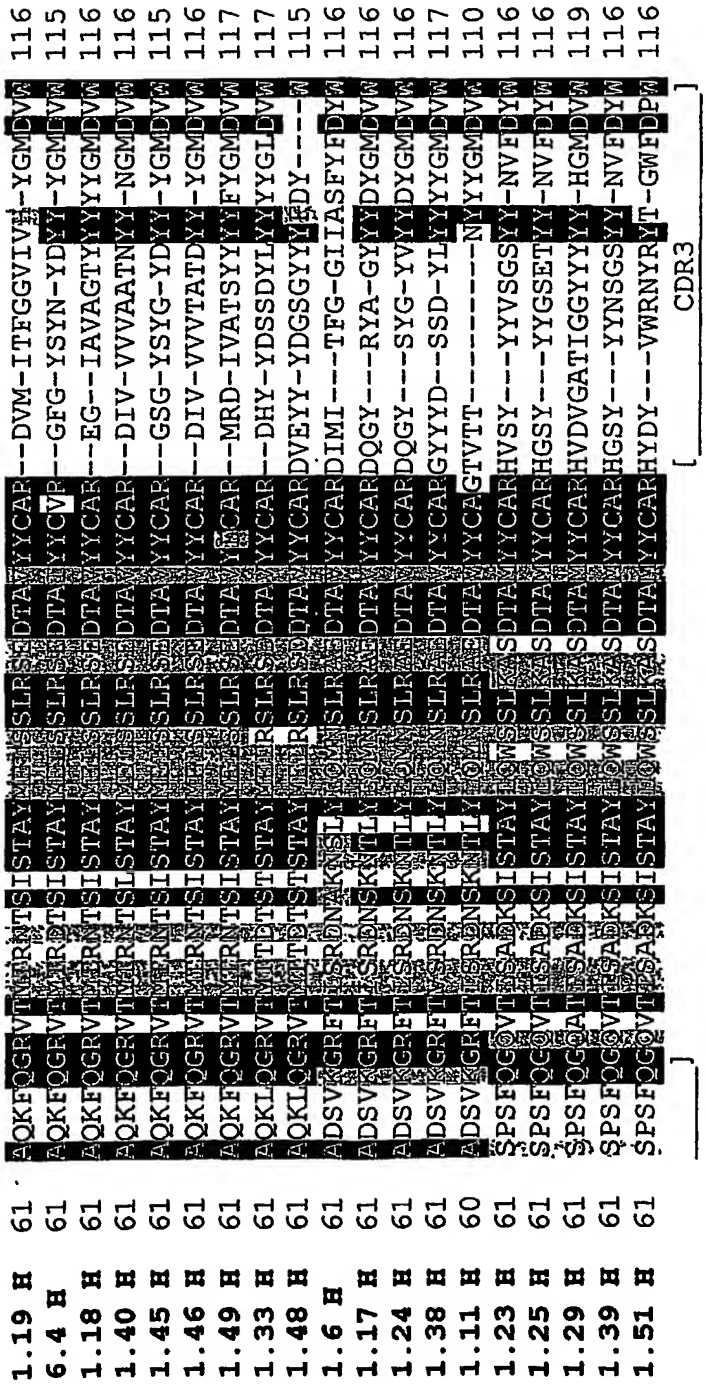

FIG. 48B

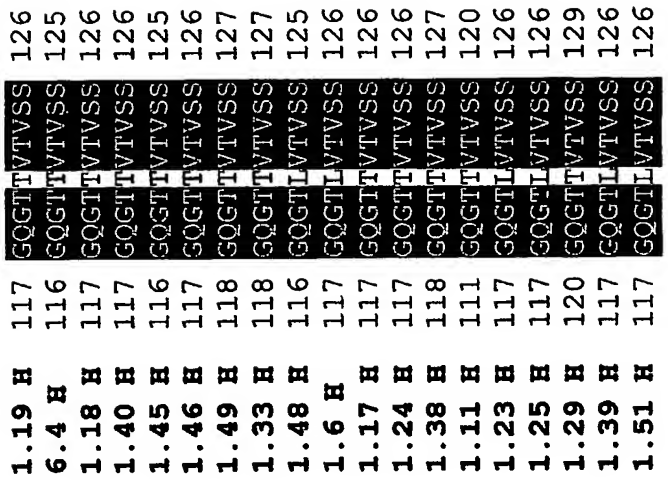
1.19 H 117 GQGTTVTVSS 126
6.4 H 116 GQGTTVTVSS 125
1.18 H 117 GQGTTVTVSS 126
1.40 H 117 GQGTTVTVSS 126
1.45 H 116 GQGTTVTVSS 125
1.46 H 117 GQGTTVTVSS 126
1.49 H 118 GQGTTVTVSS 127
1.33 H 118 GQGTTVTVSS 127
1.48 H 116 GQGTLVTVSS 125
1.6 H 117 GQGTLVTVSS 126
1.17 H 117 GQGTTVTVSS 126
1.24 H 117 GQGTTVTVSS 126
1.38 H 118 GQGTTVTVSS 127
1.11 H 111 GQGTTVTVSS 120
1.23 H 117 GQGTLVTVSS 126
1.25 H 117 GQGTLVTVSS 126
1.29 H 120 GQGTTVTVSS 129
1.39 H 117 GQGTLVTVSS 126
1.51 H 117 GQGTLVTVSS 126

FIG. 48C

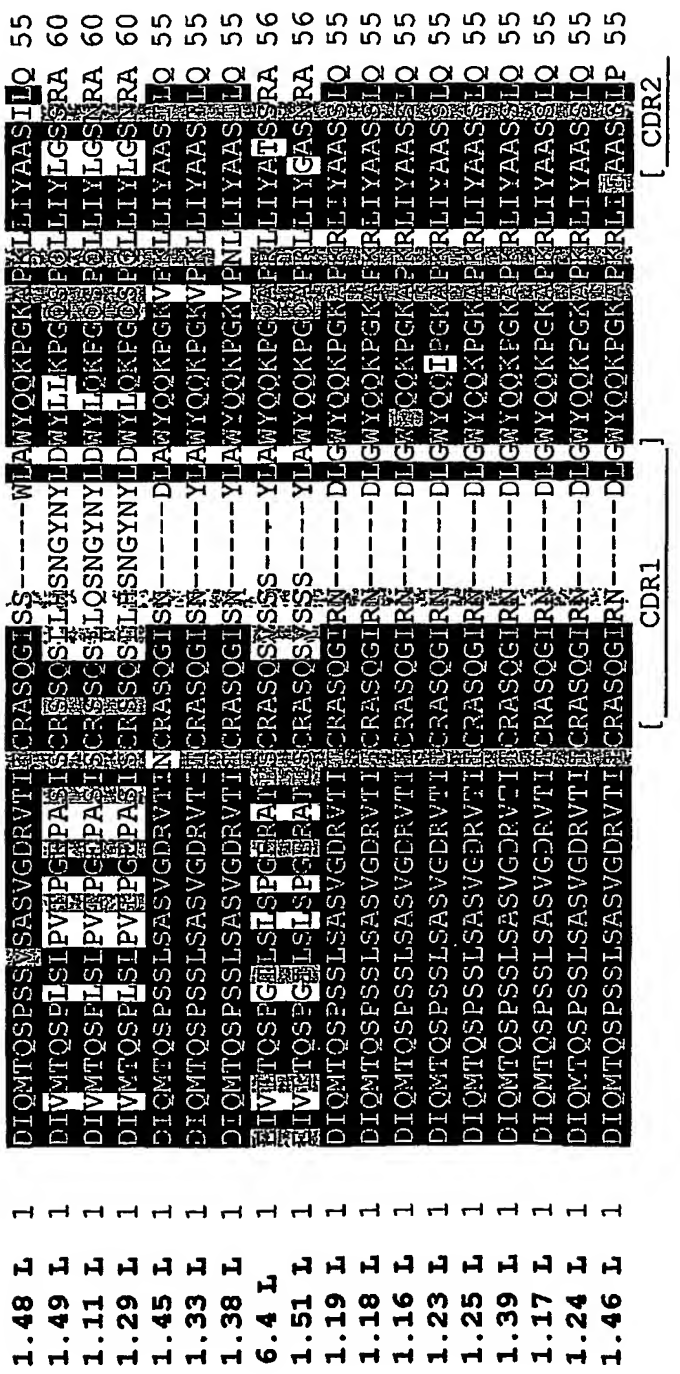

FIG. 49A

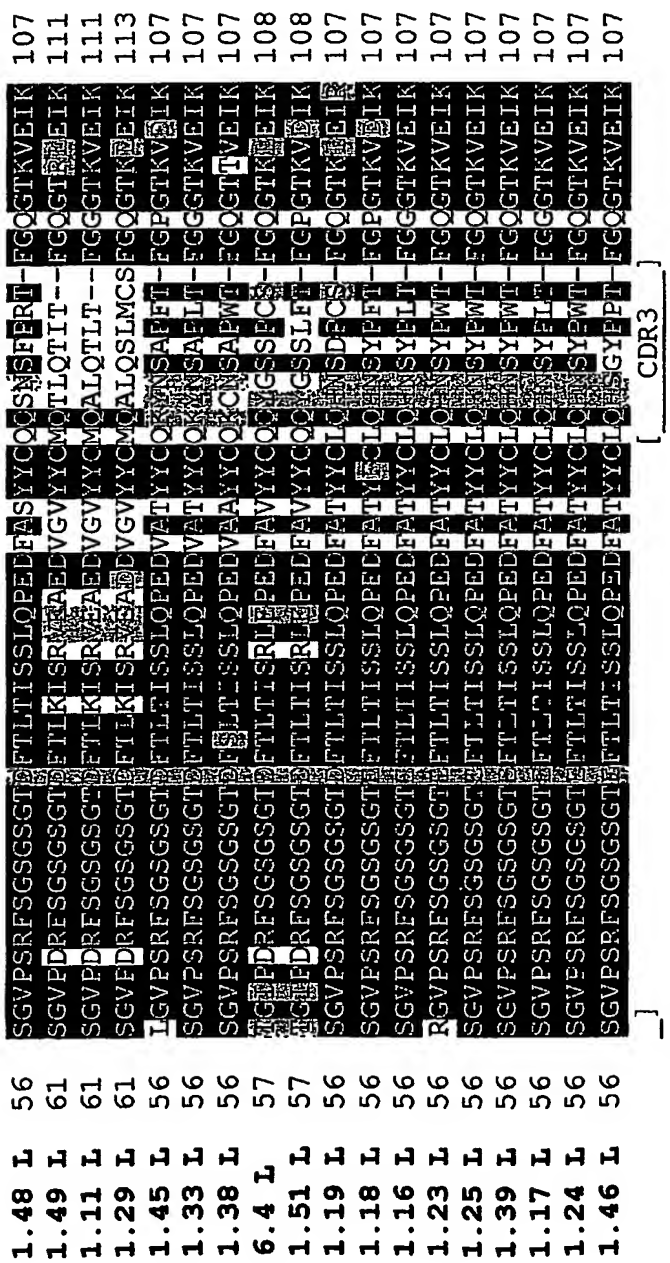

FIG. 49B

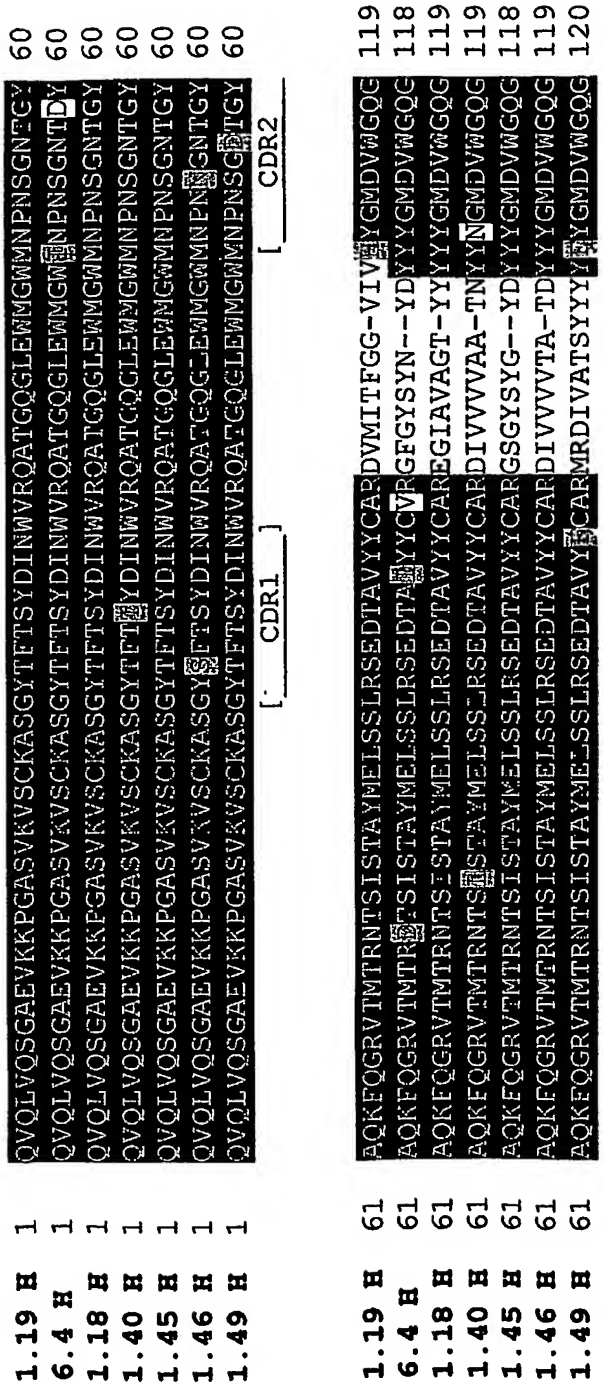
1.19 H 1 QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDINWVRQATGQGLEWMGWMNPNSGNTGY 60
6.4 H 1 QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDINWVRQATGQGLEWMGWMNPNSGNTDY 60
1.18 H 1 QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDINWVRQATGQGLEWMGWMNPNSGNTGY 60
1.40 H 1 QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDINWVRQATGQGLEWMGWMNPNSGNTGY 60
1.45 H 1 QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDINWVRQATGQGLEWMGWMNPNSGNTGY 60
1.46 H 1 QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDINWVRQATGQGLEWMGWMNPNSGNTGY 60
1.49 H 1 QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDINWVRQATGQGLEWMGWMNPNSGNTGY 60
CDR1
CDR2
1.19 H 61 AQKFQGRVTMTRNTSISTAYMELSSLRSEDTAVYYCARDVMITFGG-VIVYGMDVWGQG 119
6.4 H 61 AQKFQGRVTMTRNTSISTAYMELSSLRSEDTAVYYCVRGFGYSYN--YDYYYGMDVWGQG 118
1.18 H 61 AQKFQGRVTMTRNTSISTAYMELSSLRSEDTAVYYCAREGIAVAGT-YYYYYGMDVWGQG 119
1.40 H 61 AQKFQGRVTMTRNTSISTAYMELSSLRSEDTAVYYCARDIVVVVAA-TNYYNGMDVWGQG 119
1.45 H 61 AQKFQGRVTMTRNTSISTAYMELSSLRSEDTAVYYCARGSGYSYG--YDYYYGMDVWGQG 118
1.46 H 61 AQKFQGRVTMTRNTSISTAYMELSSLRSEDTAVYYCARDIVVVVTA-TDYYYYGMDVWGQG 119
1.49 H 61 AQKFQGRVTMTRNTSISTAYMELSSLRSEDTAVYYCARMRDIVATSYYYYYGMDVWGQG 120
CDR3
1.19 H 120 TTVTVSS 126
6.4 H 119 TTVTVSS 125
1.18 H 120 TTVTVSS 126
1.40 H 120 TTVTVSS 126
1.45 H 119 TTVTVSS 125
1.46 H 120 TTVTVSS 126
1.49 H 121 TTVTVSS 127

FIG. 50

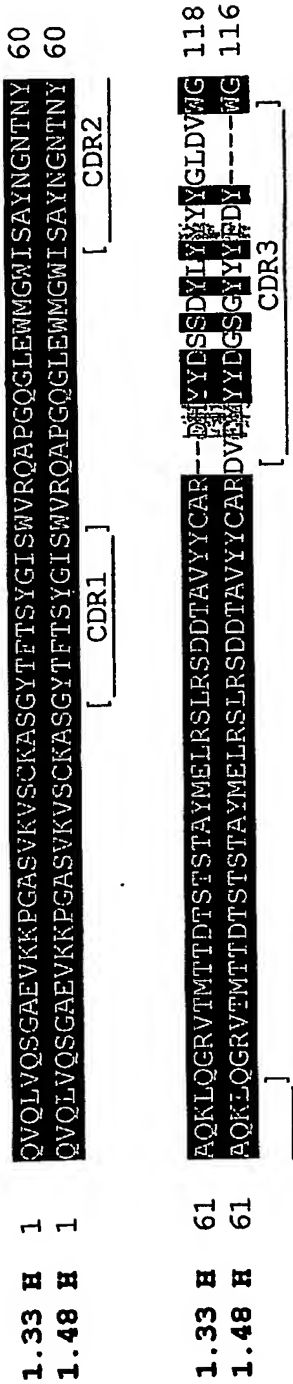
1.33 H 1 QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYGISWVRQAPGQGLEWMGWISAYNGNTNY 60
1.48 H 1 QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYGISWVRQAPGQGLEWMGWISAYNGNTNY 60
CDR1
CDR2
1.33 H 61 AQKLQGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCAR--DMFVYDSSDYLYYYGLDVWG 118
1.48 H 61 AQKLQGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARDVRRRAYYDGSGVYYFFDY---WG 116
CDR3
1.33 H 119 QGTTVTVSS 127
1.48 H 117 QGTLVTVSS 125

FIG. 51

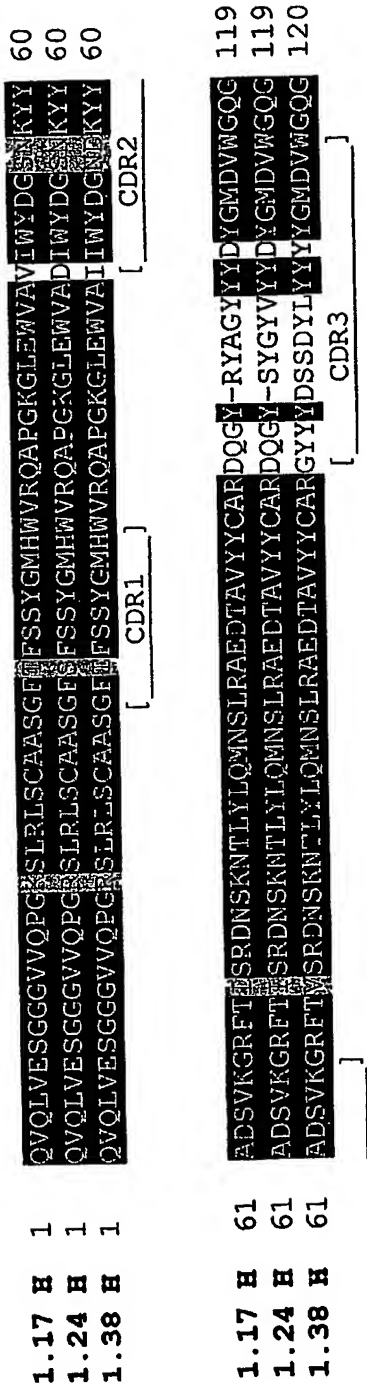
1.17 H 1 QVQLVESGGGVVQPGSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVIWYDGSNKYY 60
1.24 H 1 QVQLVESGGGVVQPGSLRLSCAASGFSFSSYGMHWVRQAPGKGLEWVADIWYDGSNKYY 60
1.38 H 1 QVQLVESGGGVVQPGSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAIIWYDGSNEKYY 60
CDR1
CDR2
1.17 H 61 ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDQGY-RYAGYYYDYGMDVWGQG 119
1.24 H 61 ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDQGY-SYGYVYYDYGMDVWGQG 119
1.38 H 61 ADSVKGRFTVSRDNSKNTLYLQMNSLRAEDTAVYYCARGYYYDSSDYLYYYGMDVWGQG 120
CDR3
1.17 H 120 TTVTVSS 126
1.24 H 120 TTVTVSS 126
1.38 H 121 TTVTVSS 127

FIG. 52

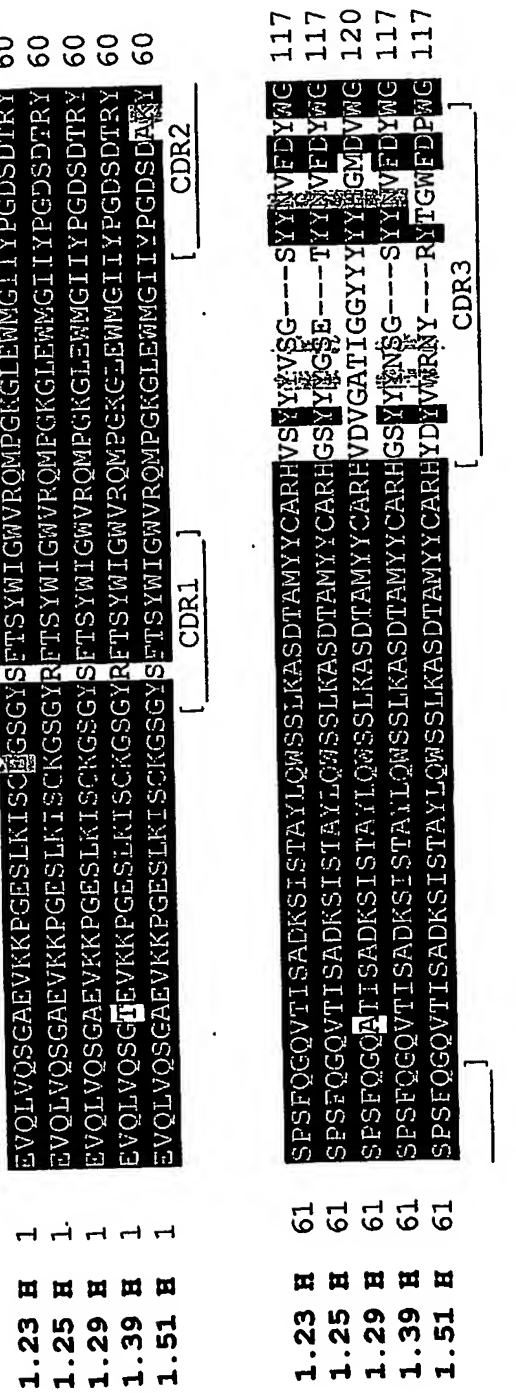

FIG. 53

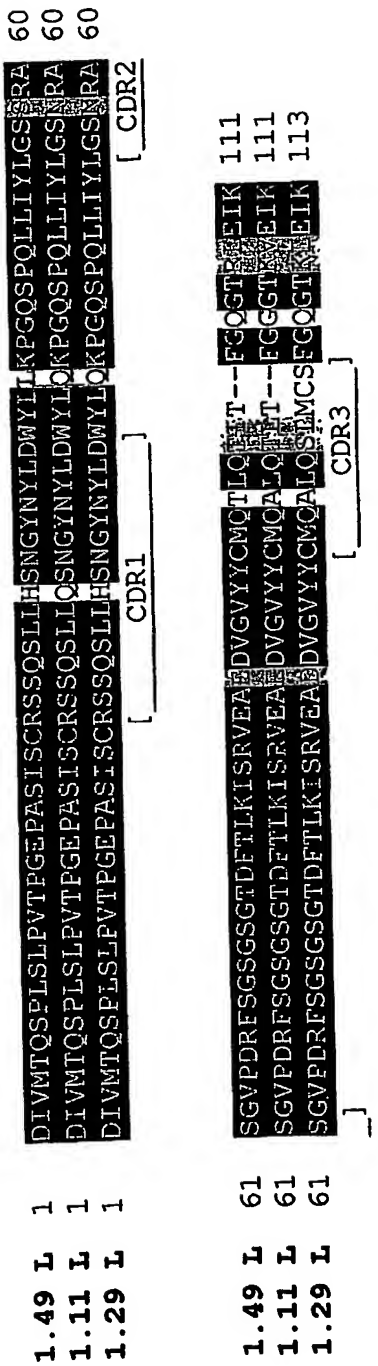
1.49 L 1 DIVMTQSPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLKPGQSPQLLIYLGS 60
1.11 L 1 DIVMTQSPLSLPVTPGEPASISCRSSQSLLQSNGYNYLDWYLQKPGQSPQLLIYLGS 60
1.29 L 1 DIVMTQSPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQLLIYLGS 60
CDR1
CDR2
1.49 L 61 SGVPDRFSGSGSGTDFTLKISRVEADDVGVYYCMQTLQTPT--FGQGTDLEIK 111
1.11 L 61 SGVPDRFSGSGSGTDFTLKISRVEADDVGVYYCMQALQTPT--FGGGTKVEIK 111
1.29 L 61 SGVPDRFSGSGSGTDFTLKISRVEADDVGVYYCMQALQSPMCSFGQGTKLEIK 113
CDR3

FIG. 54

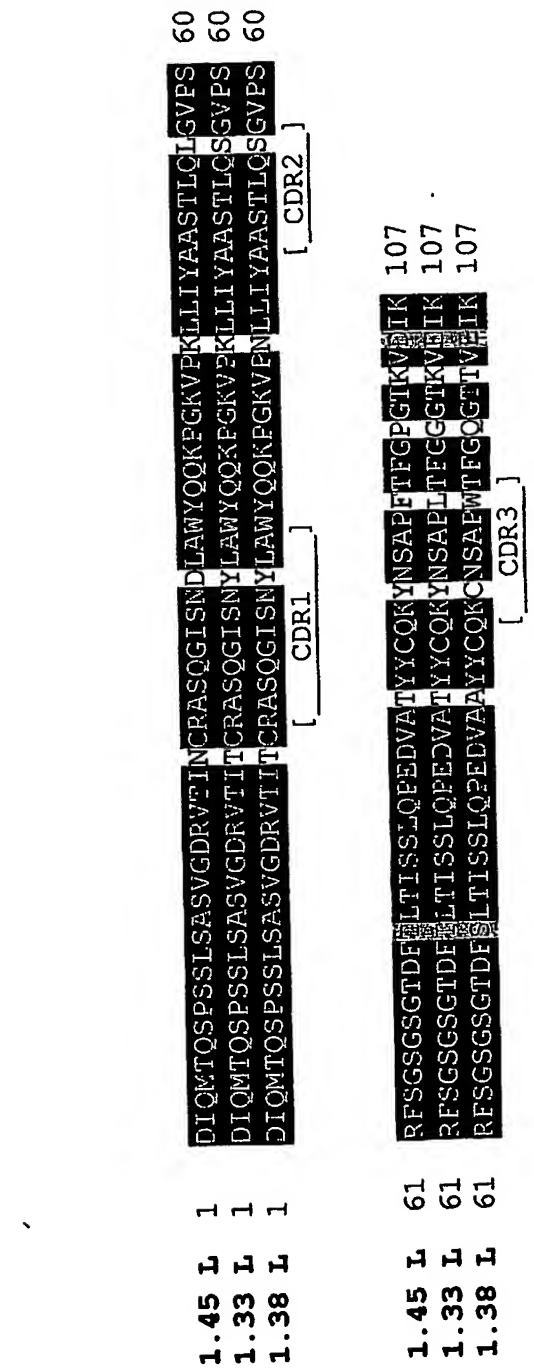
1.45 L 1 DIQMTQSPSSLSASVGDRVTINCRASQGISNDLAWYQQKPGKVPKLLIYAASTLQLGVPS 60
1.33 L 1 DIQMTQSPSSLSASVGDRVTITCRASQGISNYLAWYQQKPGKVPKLLIYAASTLQSGVPS 60
1.38 L 1 DIQMTQSPSSLSASVGDRVTITCRASQGISNYLAWYQQKPGKVPNLLIYAASTLQSGVPS 60
CDR1
CDR2
1.45 L 61 RFSGSGSGTDFTLTISSLQPEDVATYYCQKYNSAPFTFGPGTKVDIK 107
1.33 L 61 RFSGSGSGTDFTLTISSLQPEDVATYYCQKYNSAPLTFGGGTKVEIK 107
1.38 L 61 RFSGSGSGTDFTLTISSLQPEDVAAYYCQKCNSAPWTFGQGTTVEIK 107
CDR3

FIG. 55

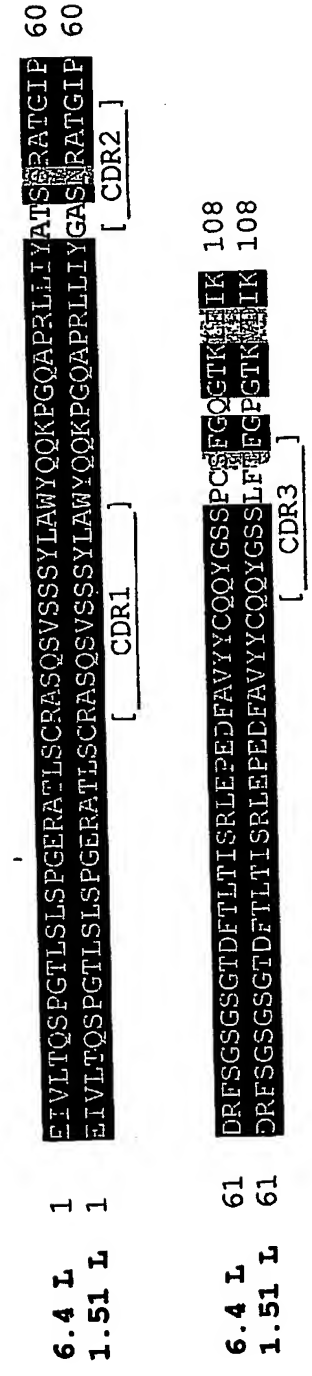
6.4 L 1 EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYATSGRATGIP 60
1.51 L 1 EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASNRATGIP 60
CDR1
CDR2
6.4 L 61 DRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSPCSFGQGTKVEIK 108
1.51 L 61 DRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSLFTFGPGTKVDIK 108
CDR3

FIG. 56

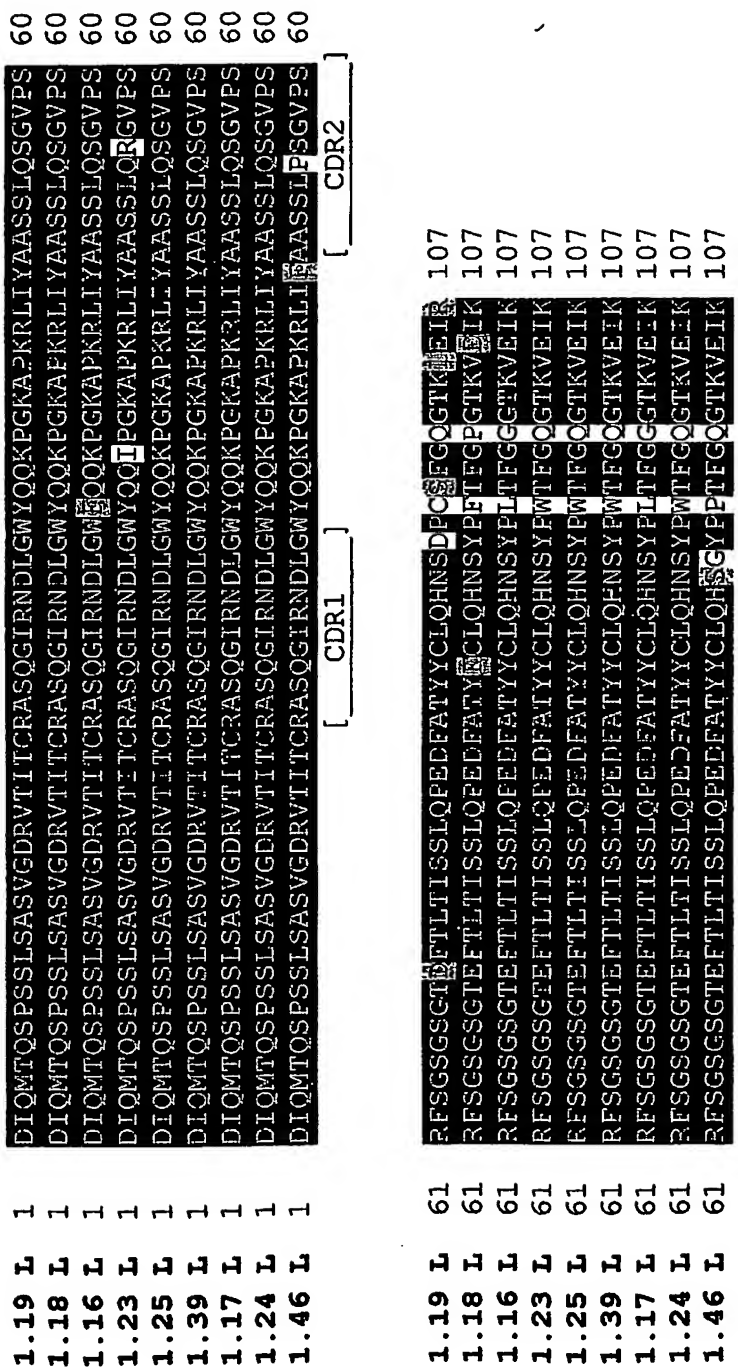
1.19 L 1 DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPGKAPKRLIYAASSLQSGVPS 60
1.18 L 1 DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPGKAPKRLIYAASSLQSGVPS 60
1.16 L 1 DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWQQKPGKAPKRLIYAASSLQSGVPS 60
1.23 L 1 DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQIPGKAPKRLIYAASSLQRGVPS 60
1.25 L 1 DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPGKAPKRLIYAASSLQSGVPS 60
1.39 L 1 DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPGKAPKRLIYAASSLQSGVPS 60
1.17 L 1 DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPGKAPKRLIYAASSLQSGVPS 60
1.24 L 1 DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPGKAPKRLIYAASSLQSGVPS 60
1.46 L 1 DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPGKAPKRLIYAASSLQSGVPS 60
CDR1
CDR2
1.19 L 61 RFSGSGSGTEFTLTISSLQPEDFATYYCLQHNSYPFTFGQGTKVEIK 107
1.18 L 61 RFSGSGSGTEFTLTISSLQPEDFATYYCLQHNSYPFTFGPGTKVDIK 107
1.16 L 61 RFSGSGSGTEFTLTISSLQFEDFATYYCLQHNSYPLTFGGGTKVEIK 107
1.23 L 61 RFSGSGSGTEFTLTISSLQPEDFATYYCLQHNSYPWTFGQGTKVEIK 107
1.25 L 61 RFSGSGSGTEFTLTISSLQPEDFATYYCLQHNSYPWTFGQGTKVEIK 107
1.39 L 61 RFSGSGSGTEFTLTISSLQPEDFATYYCLQHNSYPWTFGQGTKVEIK 107
1.17 L 61 RFSGSGSGTEFTLTISSLQPEDFATYYCLQHNSYPLTFGGGTKVEIK 107
1.24 L 61 RFSGSGSGTEFTLTISSLQPEDFATYYCLQHNSYPWTFGQGTKVEIK 107
1.46 L 61 RFSGSGSGTEFTLTISSLQPEDFATYYCLQHNSYPPTFGQGTKVEIK 107
CDR3

FIG. 57

SEQUENCE LISTING

<110> ABGENIX, INC.
CORVALAN, Jose, R.F.
JIA, Xiao-Chi
FENG, Xiao
YANG, Xiao-Dong
CHEN, Francine
GAZIT, Gadi
WEBER, Richard
BEZABEH, Binyam

<120> ANTIBODIES DIRECTED TO PDGFD AND USES THEREOF

<130> ABGENIX.051VPC

<140> US 10/041,860
<141> 2002-01-07

<160> 377

<170> FastSEQ for Windows Version 4.0

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20 25 30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Gly

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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
50 55 60
Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr

65 70 75 80
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg

<210> 3
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<212> PRT
<213> homo sapiens

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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30
Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg

<210> 4
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<212> PRT
<213> homo sapiens

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20 25 30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ala Val Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg

<210> 5
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<212> PRT
<213> homo sapiens

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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Ile Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Val Ser Ser Asn
20 25 30

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Tyr Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ser Val Ile Tyr Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
    50                  55                  60
Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu
65                  70                  75                  80
Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95
Arg
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Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
            20                  25                  30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
    50                  55                  60
Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95
Ala Arg
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<213> homo sapiens

<400> 7

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 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp
            20                  25                  30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Ser Phe Pro
                85                  90                  95
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<213> homo sapiens

<400> 8

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Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
            20                  25                  30
Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45
Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
    50                  55                  60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
                85                  90                  95
Leu Gln Thr Pro
            100
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<212> PRT
<213> homo sapiens

<400> 9

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 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Asn Tyr
            20                  25                  30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Val Ala Thr Tyr Tyr Cys Gln Lys Tyr Asn Ser Ala Pro
                85                  90                  95
```

<210> 10
<211> 96
<212> PRT
<213> homo sapiens

<400> 10

```
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
 1               5                  10                  15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
            20                  25                  30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35                  40                  45
Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    50                  55                  60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65                  70                  75                  80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
                85                  90                  95
```

<210> 11
<211> 95
<212> PRT
<213> homo sapiens

<400> 11

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
            20                  25                  30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro
                85                  90                  95
```

<210> 12
<211> 381
<212> PRT
<213> homo sapiens

<400> 12

```
Pro Met His Arg Leu Ile Phe Val Tyr Thr Leu Ile Cys Ala Asn Phe
 1               5                  10                  15
Cys Ser Cys Arg Asp Thr Ser Ala Thr Pro Gln Ser Ala Ser Ile Lys
            20                  25                  30
Ala Leu Arg Asn Ala Asn Leu Arg Arg Asp Glu Ser Asn His Leu Thr
        35                  40                  45
Asp Leu Tyr Arg Arg Asp Glu Thr Ile Gln Val Lys Gly Asn Gly Tyr
    50                  55                  60
Val Gln Ser Pro Arg Phe Pro Asn Ser Tyr Pro Arg Asn Leu Leu Leu
65                  70                  75                  80
Thr Trp Arg Leu His Ser Gln Glu Asn Thr Arg Ile Gln Leu Val Phe
                85                  90                  95
Asp Asn Gln Phe Gly Leu Glu Glu Ala Glu Asn Asp Ile Cys Arg Tyr
            100                 105                 110
Asp Phe Val Glu Val Glu Asp Ile Ser Glu Thr Ser Thr Ile Ile Arg
        115                 120                 125
Gly Arg Trp Cys Gly His Lys Glu Val Pro Pro Arg Ile Lys Ser Arg
    130                 135                 140
Thr Asn Gln Ile Lys Ile Thr Phe Lys Ser Asp Asp Tyr Phe Val Ala
145                 150                 155                 160
Leu Ala Lys Pro Gly Phe Lys Ile Tyr Tyr Ser Leu Leu Glu Asp Phe
                165                 170                 175
Gln Pro Ala Ala Ala Ser Glu Thr Asn Trp Glu Ser Val Thr Ser Ser
            180                 185                 190
Ile Ser Gly Val Ser Tyr Asn Ser Pro Ser Val Thr Asp Pro Thr Leu
        195                 200                 205
Ile Ala Asp Ala Leu Asp Lys Lys Ile Ala Glu Phe Asp Thr Val Glu
    210                 215                 220
Asp Leu Leu Lys Tyr Phe Asn Pro Glu Ser Trp Gln Glu Asp Leu Glu
225                 230                 235                 240
Asn Met Tyr Leu Asp Thr Pro Arg Tyr Arg Gly Arg Ser Tyr His Asp
                245                 250                 255
Arg Lys Ser Lys Val Ala Ser Pro Leu Asp Arg Leu Asn Asp Asp Ala
            260                 265                 270
Lys Arg Tyr Ser Cys Thr Pro Arg Asn Tyr Ser Val Ala Ser Asn Ile
        275                 280                 285
Arg Glu Glu Leu Lys Leu Ala Asn Val Val Phe Phe Pro Arg Cys Leu
    290                 295                 300
Leu Val Gln Arg Cys Gly Gly Asn Cys Gly Cys Gly Thr Val Ala Ser
305                 310                 315                 320
Asn Trp Arg Ser Cys Thr Cys Asn Ser Gly Lys Thr Val Lys Lys Tyr
```

```
                325                 330                 335
His Glu Val Leu Gln Phe Glu Pro Gly His Ile Lys Arg Arg Gly Arg
            340                 345                 350
Ala Lys Thr Met Ala Leu Val Ala Ser Pro Ile Gln Leu Asp His His
        355                 360                 365
Glu Arg Cys Asp Cys Ile Cys Ser Ser Arg Pro Pro Arg
    370                 375                 380
```

<210> 13
<211> 126
<212> PRT
<213> homo sapiens

<400> 13

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
 1               5                  10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Phe Arg Thr Tyr
            20                  25                  30
Asn Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ser Ser Ile Ser Ser Ser Ser Ser Ser Asn Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Asp Ile Met Ile Thr Phe Gly Gly Ile Ile Ala Ser Phe Tyr
            100                 105                 110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120                 125
```

<210> 14
<211> 107
<212> PRT
<213> homo sapiens

<400> 14

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
            20                  25                  30
Leu Gly Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Leu
                85                  90                  95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105
```

<210> 15
<211> 120
<212> PRT
<213> homo sapiens

<400> 15

```
Glu Val Gln Leu Val Gln Ser Gly Gly Gly Leu Ile Gln Pro Gly Gly
 1               5                  10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Val Ser Ser Asn
            20                  25                  30
Tyr Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ser Val Ile Tyr Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
    50                  55                  60
Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu
65                  70                  75                  80
Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95
Gly Thr Val Thr Thr Asn Tyr Tyr Tyr Gly Met Asp Val Trp Gly Gln
            100                 105                 110
Gly Thr Thr Val Thr Val Ser Ser
        115                 120
```

<210> 16
<211> 111
<212> PRT
<213> homo sapiens

<400> 16

```
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
 1               5                  10                  15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu Gln Ser
            20                  25                  30
Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45
Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
    50                  55                  60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
                85                  90                  95
Leu Gln Thr Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105                 110
```

<210> 17
<211> 126
<212> PRT
<213> homo sapiens

<400> 17

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Lys
 1               5                  10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ala Val Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Asp Gln Gly Tyr Arg Tyr Ala Gly Tyr Tyr Tyr Asp Tyr Gly
            100                 105                 110
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
```

115 120 125

<210> 18
<211> 107
<212> PRT
<213> homo sapiens

<400> 18
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
20 25 30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Leu
85 90 95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 19
<211> 126
<212> PRT
<213> homo sapiens

<400> 19
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Glu Gly Ile Ala Val Ala Gly Thr Tyr Tyr Tyr Tyr Tyr Gly
100 105 110
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 20
<211> 107
<212> PRT
<213> homo sapiens

<400> 20
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
20 25 30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45

```
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Phe Cys Leu Gln His Asn Ser Tyr Pro Phe
                85                  90                  95
Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
            100                 105
```

<210> 21
<211> 126
<212> PRT
<213> homo sapiens

<400> 21

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1               5                  10                  15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
Gly Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe
    50                  55                  60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Asp Val Met Ile Thr Phe Gly Gly Val Ile Val His Tyr Gly
            100                 105                 110
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

<210> 22
<211> 107
<212> PRT
<213> homo sapiens

<400> 22

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
            20                  25                  30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Asp Pro Cys
                85                  90                  95
Ser Phe Gly Gln Gly Thr Lys Leu Glu Ile Arg
            100                 105
```

<210> 23
<211> 126
<212> PRT
<213> homo sapiens

<400> 23
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15
Ser Leu Lys Ile Ser Cys Glu Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
50 55 60
Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95
Ala Arg His Val Ser Tyr Tyr Tyr Val Ser Gly Ser Tyr Tyr Asn Val
100 105 110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 24
<211> 107
<212> PRT
<213> homo sapiens

<400> 24
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
20 25 30
Leu Gly Trp Tyr Gln Gln Ile Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45
Tyr Ala Ala Ser Ser Leu Gln Arg Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Trp
85 90 95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 25
<211> 126
<212> PRT
<213> homo sapiens

<400> 25
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Phe Ser Ser Tyr
20 25 30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ala Asp Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Gln Gly Tyr Ser Tyr Gly Tyr Val Tyr Tyr Asp Tyr Gly
100 105 110

Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 26
<211> 107
<212> PRT
<213> homo sapiens

<400> 26
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
20 25 30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Trp
85 90 95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 27
<211> 126
<212> PRT
<213> homo sapiens

<400> 27
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Arg Phe Thr Ser Tyr
20 25 30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
50 55 60
Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95
Ala Arg His Gly Ser Tyr Tyr Tyr Gly Ser Glu Thr Tyr Tyr Asn Val
100 105 110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 28
<211> 107
<212> PRT
<213> homo sapiens

<400> 28
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
20 25 30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile

```
        35                  40                  45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Trp
                85                  90                  95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105
```

<210> 29
<211> 129
<212> PRT
<213> homo sapiens

<400> 29

```
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
 1               5                  10                  15
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
            20                  25                  30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
    50                  55                  60
Gln Gly Gln Ala Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95
Ala Arg His Val Asp Val Gly Ala Thr Ile Gly Gly Tyr Tyr Tyr Tyr
            100                 105                 110
Tyr His Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser
        115                 120                 125
Ser
```

<210> 30
<211> 113
<212> PRT
<213> homo sapiens

<400> 30

```
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
 1               5                  10                  15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
            20                  25                  30
Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45
Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
    50                  55                  60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80
Ser Arg Val Glu Ala Asp Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
                85                  90                  95
Leu Gln Ser Leu Met Cys Ser Phe Gly Gln Gly Thr Lys Leu Glu Ile
            100                 105                 110
Lys
```

<210> 31
<211> 127
<212> PRT
<213> homo sapiens

<400> 31
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
50 55 60
Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp His Tyr Tyr Asp Ser Ser Asp Tyr Leu Tyr Tyr Tyr Tyr
100 105 110
Gly Leu Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 32
<211> 107
<212> PRT
<213> homo sapiens

<400> 32
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Asn Tyr
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile
35 40 45
Tyr Ala Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Val Ala Thr Tyr Tyr Cys Gln Lys Tyr Asn Ser Ala Pro Leu
85 90 95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 33
<211> 127
<212> PRT
<213> homo sapiens

<400> 33
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ala Ile Ile Trp Tyr Asp Gly Asn Asp Lys Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Val Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr

```
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Gly Tyr Tyr Tyr Asp Ser Ser Asp Tyr Leu Tyr Tyr Tyr Tyr
            100                 105                 110
Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

<210> 34
<211> 107
<212> PRT
<213> homo sapiens

<400> 34

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Asn Tyr
            20                  25                  30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Asn Leu Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Ser Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Val Ala Ala Tyr Tyr Cys Gln Lys Cys Asn Ser Ala Pro Trp
                85                  90                  95
Thr Phe Gly Gln Gly Thr Thr Val Glu Ile Lys
            100                 105
```

<210> 35
<211> 126
<212> PRT
<213> homo sapiens

<400> 35

```
Glu Val Gln Leu Val Gln Ser Gly Thr Glu Val Lys Lys Pro Gly Glu
 1               5                  10                  15
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Arg Phe Thr Ser Tyr
            20                  25                  30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
    50                  55                  60
Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95
Ala Arg His Gly Ser Tyr Tyr Tyr Asn Ser Gly Ser Tyr Tyr Asn Val
            100                 105                 110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120                 125
```

<210> 36
<211> 107
<212> PRT
<213> homo sapiens

<400> 36

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
            20                  25                  30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Trp
                85                  90                  95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105
```

<210> 37
<211> 126
<212> PRT
<213> homo sapiens

```
<400> 37
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1               5                  10                  15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Thr Tyr
            20                  25                  30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
Gly Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe
    50                  55                  60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Leu Ser Thr Ala Tyr
65                  70                  75                  80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Asp Ile Val Val Val Val Ala Ala Thr Asn Tyr Tyr Asn Gly
            100                 105                 110
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

<210> 38
<211> 125
<212> PRT
<213> homo sapiens

```
<400> 38
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1               5                  10                  15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
Gly Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe
    50                  55                  60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Gly Ser Gly Tyr Ser Tyr Gly Tyr Asp Tyr Tyr Tyr Gly Met
            100                 105                 110
Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
```

115 120 125

<210> 39
<211> 107
<212> PRT
<213> homo sapiens

<400> 39
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Asn Cys Arg Ala Ser Gln Gly Ile Ser Asn Asp
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile
35 40 45
Tyr Ala Ala Ser Thr Leu Gln Leu Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Val Ala Thr Tyr Tyr Cys Gln Lys Tyr Asn Ser Ala Pro Phe
85 90 95
Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
100 105

<210> 40
<211> 126
<212> PRT
<213> homo sapiens

<400> 40
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Met Asn Pro Asn Asn Gly Asn Thr Gly Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Ile Val Val Val Val Thr Ala Thr Asp Tyr Tyr Tyr Gly
100 105 110
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 41
<211> 107
<212> PRT
<213> homo sapiens

<400> 41
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
20 25 30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45

```
Phe Ala Ala Ser Ser Leu Pro Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Ser Gly Tyr Pro Pro
                85                  90                  95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105
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<210> 42
<211> 125
<212> PRT
<213> homo sapiens

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<400> 42
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1               5                  10                  15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30
Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
    50                  55                  60
Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Asp Val Glu Tyr Tyr Tyr Asp Gly Ser Gly Tyr Tyr Tyr Phe
            100                 105                 110
Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120                 125
```

<210> 43
<211> 107
<212> PRT
<213> homo sapiens

```
<400> 43
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp
            20                  25                  30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Ile Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Ser Tyr Tyr Cys Gln Gln Ser Asn Ser Phe Pro Arg
                85                  90                  95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105
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<210> 44
<211> 127
<212> PRT
<213> homo sapiens

<400> 44
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Met Asn Pro Asn Ser Gly Asp Thr Gly Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys
85 90 95
Ala Arg Met Arg Asp Ile Val Ala Thr Ser Tyr Tyr Tyr Tyr Phe Tyr
100 105 110
Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 45
<211> 111
<212> PRT
<213> homo sapiens

<400> 45
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
20 25 30
Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Leu Lys Pro Gly Gln Ser
35 40 45
Pro Gln Leu Leu Ile Tyr Leu Gly Ser Ser Arg Ala Ser Gly Val Pro
50 55 60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Thr
85 90 95
Leu Gln Thr Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
100 105 110

<210> 46
<211> 126
<212> PRT
<213> homo sapiens

<400> 46
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Ala Lys Tyr Ser Pro Ser Phe
50 55 60
Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95
Ala Arg His Tyr Asp Tyr Val Trp Arg Asn Tyr Arg Tyr Thr Gly Trp
100 105 110

```
Phe Asp Pro Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120                 125


<210> 47
<211> 108
<212> PRT
<213> homo sapiens

<400> 47
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
 1               5                  10                  15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
            20                  25                  30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35                  40                  45
Ile Tyr Gly Ala Ser Asn Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    50                  55                  60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65                  70                  75                  80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Leu
                85                  90                  95
Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
            100                 105


<210> 48
<211> 125
<212> PRT
<213> homo sapiens

<400> 48
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1               5                  10                  15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
Gly Trp Ile Asn Pro Asn Ser Gly Asn Thr Asp Tyr Ala Gln Lys Phe
    50                  55                  60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Ile Tyr Tyr Cys
                85                  90                  95
Val Arg Gly Phe Gly Tyr Ser Tyr Asn Tyr Asp Tyr Tyr Tyr Gly Met
            100                 105                 110
Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125


<210> 49
<211> 108
<212> PRT
<213> homo sapiens

<400> 49
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
 1               5                  10                  15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
            20                  25                  30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
```

```
        35                  40                  45
Ile Tyr Ala Thr Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    50                  55                  60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65                  70                  75                  80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
                85                  90                  95
Cys Ser Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105
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<210> 50
<211> 1828
<212> DNA
<213> homo sapiens

<400> 50
ctaaaaaata tgttctctac aacaccaagg ctcattaaaa tattttaaat attaatatac 60
atttcttctg tcagaaatac ataaaacttt attatatcag cgcagggcgg cgcggcgtcg 120
gtcccgggag cagaacccgg ctttttcttg gagcgacgct gtctctagtc gctgatccca 180
aatgcaccgg ctcatctttg tctacactct aatctgcgca aacttttgca gctgtcggga 240
cacttctgca accccgcaga gcgcatccat caaagctttg cgcaacgcca acctcaggcg 300
agatgagagc aatcacctca cagacttgta ccgaagagat gagaccatcc aggtgaaagg 360
aaacggctac gtgcagagtc ctagattccc gaacagctac cccaggaacc tgctcctgac 420
atggcggctt cactctcagg agaatacacg gatacagcta gtgtttgaca atcagtttgg 480
attagaggaa gcagaaaatg atatctgtag gtatgatttt gtggaagttg aagatatatc 540
cgaaaccagt accattatta gaggacgatg gtgtggacac aaggaagttc ctccaaggat 600
aaaatcaaga acgaaccaaa ttaaaatcac attcaagtcc gatgactact ttgtggctaa 660
acctggattc aagatttatt attctttgct ggaagatttc caacccgcag cagcttcaga 720
gaccaactgg gaatctgtca caagctctat ttcaggggta tcctataact ctccatcagt 780
aacggatccc actctgattg cggatgctct ggacaaaaaa attgcagaat ttgatacagt 840
ggaagatctg ctcaagtact tcaatccaga gtcatggcaa gaagatcttg agaatatgta 900
tctggacacc cctcggtatc gaggcaggtc ataccatgac cggaagtcaa aagttgacct 960
ggataggctc aatgatgatg ccaagcgtta cagttgcact cccaggaatt actcggtcaa 1020
tataagagaa gagctgaagt tggccaatgt ggtcttcttt ccacgttgcc tcctcgtgca 1080
gcgctgtgga ggaaattgtg gctgtggaac tgtcaactgg aggtcctgca catgcaattc 1140
agggaaaacc gtgaaaaagt atcatgaggt attacagttt gagcctggcc acatcaagag 1200
gaggggtaga gctaagacca tggctctagt tgacatccag ttggatcacc atgaacgatg 1260
tgattgtatc tgcagctcaa gaccacctcg ataagagaat gtgcacatcc ttacattaag 1320
cctgaaagaa cctttagttt aaggagggtg agataagaga ccctttcct accagcaacc 1380
aaacttacta ctagcctgca atgcaatgaa cacaagtggt tgctgagtct cagccttgct 1440
ttgttaatgc catggcaagt agaaaggtat atcatcaact tctataccta agaatatagg 1500
attgcattta ataatagtgt ttgaggttat atatgcacaa acacacacag aaatatattc 1560
atgtctatgt gtatatagat caaatgtttt ttttggtata tataaccagg tacaccagag 1620
cttacatatg tttgagttag actcttaaaa tcctttgcca aaataaggga tggtcaaata 1680
tatgaaacat gtctttagaa aatttaggag ataaatttat ttttaaattt tgaaacacaa 1740
aacaattttg aatcttgctc tcttaaagaa agcatcttgt atattaaaaa tcaaaagatg 1800
aggctttctt acatatacat cttagttg 1828

<210> 51
<211> 22
<212> DNA
<213> homo sapiens

<400> 51
caggtgcagc tggagcagtc gg 22

<210> 52
<211> 24
<212> DNA
<213> homo sapiens

<400> 52
gctgagggag tagagtcctg agga 24

<210> 53
<211> 19
<212> DNA
<213> homo sapiens

<400> 53
cacaccgcgg tcacatggc 19

<210> 54
<211> 20
<212> DNA
<213> homo sapiens

<400> 54
ctactctagg gcacctgtcc 20

<210> 55
<211> 379
<212> DNA
<213> homo sapiens

<400> 55
gaggtgcagc tggtggagtc tgggggaggc ctggtcaagc ctgggggGtc cctgagactc 60
tcctgtgcag cctctggatt caacttcaga acctataaca tgaactgggt ccgccaggct 120
ccagggaagg ggctggagtg ggtctcatcc attagtagta gtagtagtaa catatactac 180
gcagactcag tgaagggccg attcaccatc tccagagaca acgccaagaa ctcactgtat 240
ctgcaaatga acagcctgag agccgaggac acggctgtat attactgtgc gagagatatt 300
atgattacgt ttgggggaat tatcgcctcg ttctactttg actactgggg ccagggaacc 360
ctggtcaccg tctcctcag 379

<210> 56
<211> 322
<212> DNA
<213> homo sapiens

<400> 56
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtca gggcattaga aatgatttag gctggtttca gcagaaacca 120
gggaaagccc ctaagcgcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180
aggttcagcg gcagtggatc tgggacagaa ttcactctca caatcagcag cctgcagcct 240
gaagattttg caacttatta ctgtctacag cataatagtt acccgctcac tttcggcgga 300
gggaccaagg tggagatcaa ac 322

<210> 57
<211> 361
<212> DNA
<213> homo sapiens

<400> 57
gaggtgcagc tggtgcagtc tggaggaggc ttgatccagc ctgggggGtc cctgagactc 60
tcctgtgcag cctctgggtt caccgtcagt agcaactaca tgagctgggt ccgccaggct 120
ccagggaagg ggctggagtg ggtctcagtt atttatagcg gtggtagcac atactacgca 180
gactccgtga agggccgatt caccatctcc agagacaatt ccaagaacac gctgtatctt 240
caaatgaaca gcctgagagc cgaggacacg gccgtgtatt actgtgcggg aacggtgact 300
acgaattact actacggtat ggacgtctgg ggccaaggga ccacggtcac cgtctcctca 360
g 361

<210> 58
<211> 334
<212> DNA
<213> homo sapiens

<400> 58
gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc 60
atctcctgca ggtctagtca gagcctcctg caaagtaatg gatacaacta tttggattgg 120
tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttc taatcgggcc 180
tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc 240
agcagagtgg aggctgagga tgttggggtt tattactgca tgcaagctct acaaactctc 300
actttcggcg gagggaccaa ggtggagatc aaac 334

<210> 59
<211> 379
<212> DNA
<213> homo sapiens

<400> 59
caggtgcagc tggtggagtc ggggggaggc gtggtccagc ctgggaagtc cctgagactc 60
tcctgtgcag cgtctggatt caccttcagt agctatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggctggagtg ggtggcagtt atatggtatg atggaagtaa taaatactat 180
gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat 240
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagatcaa 300
ggatacagat atgctggtta ctactacgac tacggtatgg acgtctgggg ccaagggacc 360
acggtcaccg tctcctcag 379

<210> 60
<211> 322
<212> DNA
<213> homo sapiens

<400> 60
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtca gggcattaga aatgatttag gctggtatca gcagaaacca 120
gggaaagccc ctaagcgcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180
aggttcagcg gcagtggatc tgggacagaa ttcactctca caatcagcag cctgcagcct 240
gaagattttg caacttatta ctgtctacag cataatagtt acccgctcac tttcggcgga 300
gggaccaagg tggagatcaa ac 322

<210> 61
<211> 379
<212> DNA
<213> homo sapiens

<400> 61
caggtgcagc tggtgcagtc gggggctgag gtgaagaagc ctggggcctc agtgaaggtc 60
tcctgcaagg cttctggata caccttcacc agttatgata tcaactgggt gcgacaggcc 120
actggacaag ggcttgagtg gatgggatgg atgaacccaa acagtggtaa cacaggctat 180
gcacagaagt tccagggcag agtcaccatg accaggaaca cctccataag cacagcctac 240
atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc gagagagggt 300
atagcagtgg ctgggacata ctactactac tacggtatgg acgtctgggg ccaagggacc 360
acggtcaccg tctcctcag 379

<210> 62
<211> 322
<212> DNA
<213> homo sapiens

<400> 62
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60

atcacttgcc gggcaagtca gggcattaga aatgatttag gctggtatca gcagaaacca 120
gggaaagccc ctaagcgcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180
aggttcagcg gcagtggatc tgggacagaa ttcactctca caatcagcag cctgcagcct 240
gaagattttg caacttattt ctgtctacag cataatagtt acccattcac tttcggccct 300
gggaccaaag tggatatcaa ac 322

<210> 63
<211> 379
<212> DNA
<213> homo sapiens

<400> 63
caggtgcagc tggtgcagtc tggggctgag gtgaagaagc ctggggcctc agtgaaggtc 60
tcctgcaagg cttctggata caccttcacc agttatgata tcaactgggt gcgacaggcc 120
actggacaag ggcttgagtg gatgggatgg atgaacccta acagtggtaa cacaggctat 180
gcacagaagt tccagggcag agtcaccatg accaggaaca cctccataag cacagcctac 240
atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc gagagacgtt 300
atgattacgt ttgggggagt tatcgtgcac tacggtatgg acgtctgggg ccaagggacc 360
acggtcaccg tctcctcag 379

<210> 64
<211> 322
<212> DNA
<213> homo sapiens

<400> 64
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtca gggcattaga aatgatttag gctggtatca gcagaaacca 120
gggaaagccc ctaagcgcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180
aggttcagcg gcagtggatc tgggacagat ttcactctca caatcagcag cctgcagcct 240
gaagattttg caacttatta ctgtctacag cataatagtg acccgtgcag ttttggccag 300
gggaccaagc tggagatcag ac 322

<210> 65
<211> 379
<212> DNA
<213> homo sapiens

<400> 65
gaggtgcagc tggtgcagtc tggagcagag gtgaaaaagc ccggggagtc tctgaagatc 60
tcctgtgagg gttctggata cagctttacc agctactgga tcggctgggt gcgccagatg 120
cccgggaaag gcctggagtg gatggggatc atctatcctg gtgactctga taccagatac 180
agcccgtcct tccaaggcca ggtcaccatc tcagccgaca agtccatcag caccgcctac 240
ctgcagtgga gcagcctgaa ggcctcggac accgccatgt attactgtgc gagacatgta 300
tcgtattact atgtttcggg gagttattat aacgtctttg actactgggg ccagggaacc 360
ctggtcaccg tctcctcag 379

<210> 66
<211> 322
<212> DNA
<213> homo sapiens

<400> 66
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtca gggcattaga aatgatttag gctggtatca gcagatacca 120
gggaaagccc ctaagcgcct gatctatgct gcatccagtt tgcaacgtgg ggtcccatca 180
aggttcagcg gcagtggatc tgggacagaa ttcactctca caatcagcag cctgcagcct 240
gaagattttg caacttatta ctgtctacag cataatagtt acccgtggac gttcggccaa 300
gggaccaagg tggaaatcaa ac 322

<210> 67

<211> 379
<212> DNA
<213> homo sapiens

<400> 67
caggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
tcctgtgcag cgtctggatt cagtttcagt agctatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggctggagtg ggtggcagat atatggtatg atggaagtaa taaatactat 180
gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat 240
ctgcaaatga acagcctgag agccgaggac acggctgtgt attattgtgc gagagatcag 300
ggatacagct atggttacgt ctactacgac tacggtatgg acgtctgggg ccaagggacc 360
acggtcaccg tctcctcag 379

<210> 68
<211> 322
<212> DNA
<213> homo sapiens

<400> 68
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtca gggcattaga aatgatttag gctggtatca gcagaaacca 120
gggaaagccc ctaagcgcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180
aggttcagcg gcagtggatc tgggacagag ttcactctca caatcagcag cctgcagcct 240
gaagattttg caacttatta ctgtctacag cataatagtt acccgtggac gttcggccaa 300
gggaccaagg tggaaatcaa ac 322

<210> 69
<211> 379
<212> DNA
<213> homo sapiens

<400> 69
gaggtgcagc tggtgcagtc gggagcagag gtgaaaaagc ccggggagtc tctgaagatc 60
tcctgtaagg gttctggata caggtttacc agctactgga tcggctgggt gcgccagatg 120
cccgggaaag gcctggagtg gatggggatc atctatcctg gtgactctga taccagatac 180
agcccgtcct tccaaggcca ggtcaccatc tcagccgaca agtccatcag caccgcctac 240
ctgcagtgga gcagcctgaa ggcctcggac accgccatgt attactgtgc gagacatgga 300
tcgtattatt atggttcgga gacttattat aatgtctttg actactgggg ccagggaacc 360
ctggtcaccg tctcctcag 379

<210> 70
<211> 322
<212> DNA
<213> homo sapiens

<400> 70
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtca gggcattaga aatgatttag gctggtatca gcagaaacca 120
gggaaagccc ctaagcgcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180
aggttcagcg gcagtggatc tgggacagaa ttcactctca caatcagcag cctgcagcct 240
gaagattttg caacttatta ctgtctacag cataatagtt acccgtggac gttcggccaa 300
gggaccaagg tggaaatcaa ac 322

<210> 71
<211> 388
<212> DNA
<213> homo sapiens

<400> 71
gaggtgcagc tggtgcagtc gggagcagag gtgaaaaagc ccggggagtc tctgaagatc 60
tcctgtaagg gttctggata cagctttacc agctactgga tcggctgggt gcgccagatg 120

cccgggaaag gcctggagtg gatggggatc atctatcctg gtgactctga taccagatac 180
agcccgtcct tccaaggcca ggccaccatc tcagccgaca agtccatcag caccgcctac 240
ctgcagtgga gcagcctgaa ggcctcggac accgccatgt attactgtgc gagacacgtg 300
gatgtagggg ctacgattgg gggatattac tattactacc acggtatgga cgtctggggc 360
caagggacca cggtcaccgt ctcctcag 388

<210> 72
<211> 340
<212> DNA
<213> homo sapiens

<400> 72
gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc 60
atctcctgca ggtctagtca gagcctcctg catagtaatg gatacaacta tttggattgg 120
tacctgcaga agccagggca gtctccacaa ctcctgatct atttgggttc taatcgggcc 180
tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc 240
agcagagtgg aggctgacga tgttggggtt tattactgca tgcaagctct acaatctctc 300
atgtgcagtt ttggccaggg gaccaagctg gagatcaaac 340

<210> 73
<211> 382
<212> DNA
<213> homo sapiens

<400> 73
caggttcagc tggtgcagtc gggagctgag gtgaagaagc ctggggcctc agtgaaggtc 60
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cctggacaag ggcttgagtg gatgggatgg atcagcgctt acaatggtaa cacaaactat 180
gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagcctac 240
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gggaaagttc ctaagctcct gatctatgct gcatccactt tgcaatcagg ggtcccatct 180
cggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag cctgcagcct 240
gaagatgttg caacttatta ctgtcaaaag tataacagtg ccccgctcac tttcggcgga 300
gggaccaagg tggagatcaa ac 322

<210> 75
<211> 382
<212> DNA
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<400> 75
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ccaggcaagg ggctggagtg ggtggcaatt atatggtatg atggaaatga taaatactat 180
gcagactccg tgaagggccg cttcaccgtc tccagagaca attccaagaa cacgctgtat 240
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagaggatat 300
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accacggtca ccgtctcctc ag 382

<210> 76

<211> 322
<212> DNA
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<400> 76
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gggaccacgg tggagatcaa ac 322

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<211> 379
<212> DNA
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<400> 77
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cccgggaaag gcctggagtg gatggggatc atctatcctg gtgactctga taccagatac 180
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<210> 78
<211> 322
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gggaccaagg tggaaatcaa ac 322

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<211> 379
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gtagtggtgg tagctgctac caactactac aacggtatgg acgtctgggg ccaagggacc 360
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<211> 376
<212> DNA
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actggacaag ggcttgagtg gatgggatgg atgaacccta acagtggtaa cacaggctat 180
gcacagaagt tccagggcag agtcaccatg accaggaaca cctccataag cacagcctac 240
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ggatacagct atggttacga ctactactac ggtatggacg tctggggcca agggaccacg 360
gtcaccgtct cctcag 376

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gggaaagttc ctaagctcct gatctatgct gcatccactt tgcaattagg ggtcccatct 180
cggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag cctgcagcct 240
gaagatgttg caacttatta ctgtcaaaag tataacagtg ccccattcac tttcggccct 300
gggaccaaag tggatatcaa ac 322

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<211> 379
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actggacaag ggcttgagtg gatgggatgg atgaacccta acaatggtaa cacaggctat 180
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atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc gagagatatt 300
gtagtggtgg taactgctac ggactactac tacggtatgg acgtctgggg ccaagggacc 360
acggtcaccg tctcctcag 379

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<211> 322
<212> DNA
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gggaaagccc ctaagcgcct gatttttgct gcatccagtt tgccaagtgg ggtcccatca 180
aggttcagcg gcagtggatc tgggacagaa ttcactctca caatcagcag cctgcagcct 240
gaagattttg caacttatta ctgtctacag catagtggtt accctccgac gttcggccaa 300
gggaccaagg tggaaatcaa ac 322

<210> 84
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<212> DNA
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tcctgcaagg cttctggtta caccttacc agctatggta tcagctgggt gcgacaggcc 120
cctggacaag ggcttgagtg gatgggatgg atcagcgctt acaatggtaa cacaaactat 180
gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagcctac 240
atggagctga ggagcctgag atctgacgac acggccgtgt attactgtgc gagagatgtt 300
gaatattact atgatggtag tggttattac tactttgact actggggcca gggaaccctg 360
gtcaccgtct cctcag 376

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aggttcagcg gcagtggatc tgggacagat ttcactctca ccatcagcag cctgcagcct 240
gaggattttg catcttacta ttgtcaacag tctaacagtt tccctcggac gttcggccaa 300
gggaccaagg tggagatcaa ac 322

<210> 86
<211> 382
<212> DNA
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<400> 86
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tcctgcaagg cttctggata caccttcacc agttatgata tcaactgggt gcgacaggcc 120
actggacaag ggcttgagtg gatgggatgg atgaacccta acagtggtga cacaggctat 180
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gatatagtgg ctacgagcta ttactactac ttctacggta tggacgtctg gggccaaggg 360
accacggtca ccgtctcctc ag 382

<210> 87
<211> 334
<212> DNA
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tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc 240
agcagagtgg aggctgagga tgttggggtt tattactgca tgcaaactct acaaactatc 300
accttcggcc aagggacacg actggagatt aaac 334

<210> 88
<211> 379
<212> DNA
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<400> 88
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cccgggaaag gcctggagtg gatggggatc atctatcctg gtgactctga tgccaaatac 180
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ctgcagtgga gcagcctgaa ggcctcggac accgccatgt attactgtgc gagacactat 300
gattacgttt ggaggaatta tcggtataca gggtggttcg acccctgggg ccagggaacc 360
ctggtcaccg tctcctcag 379

<210> 89
<211> 325
<212> DNA
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<400> 89
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cctggccagg ctcccaggct cctcatctat ggtgcatcca acagggccac tggcatccca 180
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cctgaagatt ttgcagtgta ttactgtcag cagtatggta gctcactatt cactttcggc 300
cctgggacca aagtggatat caaac 325

<210> 90
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<212> DNA
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<210> 91
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<400> 92
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<210> 93
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gtggac 6

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ctacaa 6

<210> 181
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<400> 181
tctctcatgt gcag 14

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ttttgg 6

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<210> 187

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tccctc 6

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<400> 194

ggacgtt 7

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caaact 6

<210> 196
<211> 6
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<400> 196
atcacc 6

<210> 197
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<400> 197
gctcac 6

<210> 198
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<213> homo sapiens

<400> 198
attcac 6

<210> 199
<211> 126
<212> PRT
<213> homo sapiens

<400> 199

Gln	Val	Gln	Leu	Val	Gln	Ser	Gly	Ala	Glu	Val	Lys	Lys	Pro	Gly	Ala
1				5					10					15	
Ser	Val	Lys	Val	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Thr	Phe	Thr	Ser	Tyr
			20					25					30		
Asp	Ile	Asn	Trp	Val	Arg	Gln	Ala	Thr	Gly	Gln	Gly	Leu	Glu	Trp	Met
		35					40					45			
Gly	Trp	Met	Asn	Pro	Asn	Ser	Gly	Asn	Thr	Gly	Tyr	Ala	Gln	Lys	Phe
	50					55					60				
Gln	Gly	Arg	Val	Thr	Met	Thr	Arg	Asn	Thr	Ser	Ile	Ser	Thr	Ala	Tyr
65					70					75					80
Met	Glu	Leu	Ser	Ser	Leu	Arg	Ser	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
				85					90					95	
Ala	Arg	Asp	Val	Met	Ile	Thr	Phe	Gly	Gly	Val	Ile	Val	His	Tyr	Gly
			100					105					110		
Met	Asp	Val	Trp	Gly	Gln	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser		
		115					120					125			

<210> 200
<211> 125
<212> PRT

<213> homo sapiens

<400> 200
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Ile Asn Pro Asn Ser Gly Asn Thr Asp Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Ile Tyr Tyr Cys
85 90 95
Val Arg Gly Phe Gly Tyr Ser Tyr Asn Tyr Asp Tyr Tyr Tyr Gly Met
100 105 110
Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 201
<211> 126
<212> PRT
<213> homo sapiens

<400> 201
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Glu Gly Ile Ala Val Ala Gly Thr Tyr Tyr Tyr Tyr Tyr Gly
100 105 110
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 202
<211> 126
<212> PRT
<213> homo sapiens

<400> 202
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Thr Tyr
20 25 30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Leu Ser Thr Ala Tyr
65 70 75 80

```
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Asp Ile Val Val Val Val Ala Ala Thr Asn Tyr Tyr Asn Gly
            100                 105                 110
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

<210> 203
<211> 125
<212> PRT
<213> homo sapiens

<400> 203

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1               5                  10                  15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
Gly Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe
    50                  55                  60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Gly Ser Gly Tyr Ser Tyr Gly Tyr Asp Tyr Tyr Tyr Gly Met
            100                 105                 110
Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

<210> 204
<211> 126
<212> PRT
<213> homo sapiens

<400> 204

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1               5                  10                  15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Ser Tyr
            20                  25                  30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
Gly Trp Met Asn Pro Asn Asn Gly Asn Thr Gly Tyr Ala Gln Lys Phe
    50                  55                  60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Asp Ile Val Val Val Val Thr Ala Thr Asp Tyr Tyr Tyr Gly
            100                 105                 110
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

<210> 205
<211> 127
<212> PRT
<213> homo sapiens

<400> 205
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Met Asn Pro Asn Ser Gly Asp Thr Gly Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys
85 90 95
Ala Arg Met Arg Asp Ile Val Ala Thr Ser Tyr Tyr Tyr Tyr Phe Tyr
100 105 110
Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 206
<211> 117
<212> PRT
<213> homo sapiens

<400> 206
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
50 55 60
Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp His Tyr Tyr Asp Ser Ser Asp Tyr Leu Tyr Tyr Tyr Tyr
100 105 110
Gly Leu Asp Val Trp
115

<210> 207
<211> 125
<212> PRT
<213> homo sapiens

<400> 207
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
50 55 60
Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

```
Ala Arg Asp Val Glu Tyr Tyr Tyr Asp Gly Ser Gly Tyr Tyr Tyr Phe
            100                 105                 110
Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120                 125


<210> 208
<211> 126
<212> PRT
<213> homo sapiens

<400> 208
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
 1               5                  10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Phe Arg Thr Tyr
            20                  25                  30
Asn Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ser Ser Ile Ser Ser Ser Ser Ser Ser Asn Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Asp Ile Met Ile Thr Phe Gly Gly Ile Ile Ala Ser Phe Tyr
            100                 105                 110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120                 125


<210> 209
<211> 126
<212> PRT
<213> homo sapiens

<400> 209
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Lys
 1               5                  10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ala Val Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Asp Gln Gly Tyr Arg Tyr Ala Gly Tyr Tyr Tyr Asp Tyr Gly
            100                 105                 110
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125


<210> 210
<211> 126
<212> PRT
<213> homo sapiens

<400> 210
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
```

```
 1               5                  10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Phe Ser Ser Tyr
            20                  25                  30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ala Asp Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Asp Gln Gly Tyr Ser Tyr Gly Tyr Val Tyr Tyr Asp Tyr Gly
            100                 105                 110
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

<210> 211
<211> 127
<212> PRT
<213> homo sapiens

<400> 211

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
 1               5                  10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20                  25                  30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ala Ile Ile Trp Tyr Asp Gly Asn Asp Lys Tyr Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Val Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Gly Tyr Tyr Tyr Asp Ser Ser Asp Tyr Leu Tyr Tyr Tyr Tyr
            100                 105                 110
Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

<210> 212
<211> 120
<212> PRT
<213> homo sapiens

<400> 212

```
Glu Val Gln Leu Val Gln Ser Gly Gly Gly Leu Ile Gln Pro Gly Gly
 1               5                  10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Val Ser Ser Asn
            20                  25                  30
Tyr Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ser Val Ile Tyr Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
    50                  55                  60
Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu
65                  70                  75                  80
Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95
Gly Thr Val Thr Thr Asn Tyr Tyr Tyr Gly Met Asp Val Trp Gly Gln
            100                 105                 110
```

Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 213
<211> 130
<212> PRT
<213> homo sapiens

<400> 213
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15
Ser Leu Lys Ile Ser Cys Glu Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Glu Val Gln Leu
50 55 60
Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu Ser Leu Lys Ile
65 70 75 80
Ser Cys Glu Gly Ser Gly Tyr Ser Phe Thr Ser Tyr Trp Ile Gly Trp
85 90 95
Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met Gly Ile Ile Tyr
100 105 110
Pro Gly Asp Ser Asp Thr Arg Tyr Gly Gln Gly Thr Leu Val Thr Val
115 120 125
Ser Ser
130

<210> 214
<211> 126
<212> PRT
<213> homo sapiens

<400> 214
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Arg Phe Thr Ser Tyr
20 25 30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
50 55 60
Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95
Ala Arg His Gly Ser Tyr Tyr Tyr Gly Ser Glu Thr Tyr Tyr Asn Val
100 105 110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 215
<211> 129
<212> PRT
<213> homo sapiens

<400> 215
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu

```
1               5                   10                  15
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
            20                  25                  30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
    50                  55                  60
Gln Gly Gln Ala Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95
Ala Arg His Val Asp Val Gly Ala Thr Ile Gly Gly Tyr Tyr Tyr Tyr
            100                 105                 110
Tyr His Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser
        115                 120                 125
Ser
```

<210> 216
<211> 126
<212> PRT
<213> homo sapiens

<400> 216

```
Glu Val Gln Leu Val Gln Ser Gly Thr Glu Val Lys Lys Pro Gly Glu
 1               5                   10                  15
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Arg Phe Thr Ser Tyr
            20                  25                  30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
    50                  55                  60
Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95
Ala Arg His Gly Ser Tyr Tyr Tyr Asn Ser Gly Ser Tyr Tyr Asn Val
            100                 105                 110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120                 125
```

<210> 217
<211> 126
<212> PRT
<213> homo sapiens

<400> 217

```
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
 1               5                   10                  15
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
            20                  25                  30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Ala Lys Tyr Ser Pro Ser Phe
    50                  55                  60
Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95
```

Ala Arg His Tyr Asp Tyr Val Trp Arg Asn Tyr Arg Tyr Thr Gly Trp
100 105 110
Phe Asp Pro Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 218
<211> 107
<212> PRT
<213> homo sapiens

<400> 218
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45
Tyr Ala Ala Ser Ile Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Ser Tyr Tyr Cys Gln Gln Ser Asn Ser Phe Pro Arg
85 90 95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 219
<211> 111
<212> PRT
<213> homo sapiens

<400> 219
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
20 25 30
Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Leu Lys Pro Gly Gln Ser
35 40 45
Pro Gln Leu Leu Ile Tyr Leu Gly Ser Ser Arg Ala Ser Gly Val Pro
50 55 60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Thr
85 90 95
Leu Gln Thr Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
100 105 110

<210> 220
<211> 111
<212> PRT
<213> homo sapiens

<400> 220
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu Gln Ser
20 25 30
Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser

```
        35                  40                  45
Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
    50                  55                  60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
                85                  90                  95
Leu Gln Thr Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105                 110
```

<210> 221
<211> 113
<212> PRT
<213> homo sapiens

<400> 221

```
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
 1               5                  10                  15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
            20                  25                  30
Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45
Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
    50                  55                  60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80
Ser Arg Val Glu Ala Asp Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
                85                  90                  95
Leu Gln Ser Leu Met Cys Ser Phe Gly Gln Gly Thr Lys Leu Glu Ile
            100                 105                 110
Lys
```

<210> 222
<211> 107
<212> PRT
<213> homo sapiens

<400> 222

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Asn Cys Arg Ala Ser Gln Gly Ile Ser Asn Asp
            20                  25                  30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Thr Leu Gln Leu Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Val Ala Thr Tyr Tyr Cys Gln Lys Tyr Asn Ser Ala Pro Phe
                85                  90                  95
Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
            100                 105
```

<210> 223
<211> 107
<212> PRT
<213> homo sapiens

<400> 223
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Asn Tyr
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile
35 40 45
Tyr Ala Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Val Ala Thr Tyr Tyr Cys Gln Lys Tyr Asn Ser Ala Pro Leu
85 90 95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 224
<211> 107
<212> PRT
<213> homo sapiens

<400> 224
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Asn Tyr
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Asn Leu Leu Ile
35 40 45
Tyr Ala Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Ser Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Val Ala Ala Tyr Tyr Cys Gln Lys Cys Asn Ser Ala Pro Trp
85 90 95
Thr Phe Gly Gln Gly Thr Thr Val Glu Ile Lys
100 105

<210> 225
<211> 108
<212> PRT
<213> homo sapiens

<400> 225
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45
Ile Tyr Ala Thr Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
85 90 95
Cys Ser Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 226
<211> 108
<212> PRT
<213> homo sapiens

<400> 226
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45
Ile Tyr Gly Ala Ser Asn Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Leu
85 90 95
Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
100 105

<210> 227
<211> 107
<212> PRT
<213> homo sapiens

<400> 227
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
20 25 30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Asp Pro Cys
85 90 95
Ser Phe Gly Gln Gly Thr Lys Leu Glu Ile Arg
100 105

<210> 228
<211> 107
<212> PRT
<213> homo sapiens

<400> 228
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
20 25 30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

```
Glu Asp Phe Ala Thr Tyr Phe Cys Leu Gln His Asn Ser Tyr Pro Phe
                85                  90                  95
Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
            100                 105
```

<210> 229
<211> 107
<212> PRT
<213> homo sapiens

<400> 229

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
            20                  25                  30
Leu Gly Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Leu
                85                  90                  95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105
```

<210> 230
<211> 107
<212> PRT
<213> homo sapiens

<400> 230

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
            20                  25                  30
Leu Gly Trp Tyr Gln Gln Ile Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Ser Leu Gln Arg Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Trp
                85                  90                  95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105
```

<210> 231
<211> 107
<212> PRT
<213> homo sapiens

<400> 231

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
            20                  25                  30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
```

```
        35                  40                  45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Trp
                85                  90                  95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105
```

<210> 232
<211> 107
<212> PRT
<213> homo sapiens

<400> 232

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
            20                  25                  30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Trp
                85                  90                  95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105
```

<210> 233
<211> 107
<212> PRT
<213> homo sapiens

<400> 233

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
            20                  25                  30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Leu
                85                  90                  95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105
```

<210> 234
<211> 107
<212> PRT
<213> homo sapiens

<400> 234

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
            20                  25                  30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Trp
                85                  90                  95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105
```

<210> 235
<211> 107
<212> PRT
<213> homo sapiens

<400> 235

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
            20                  25                  30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35                  40                  45
Phe Ala Ala Ser Ser Leu Pro Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Ser Gly Tyr Pro Pro
                85                  90                  95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105
```

<210> 236
<211> 126
<212> PRT
<213> homo sapiens

<400> 236

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1               5                  10                  15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
Gly Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe
    50                  55                  60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Asp Val Met Ile Thr Phe Gly Gly Val Ile Val His Tyr Gly
            100                 105                 110
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

<210> 237
<211> 125
<212> PRT
<213> homo sapiens

<400> 237
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Ile Asn Pro Asn Ser Gly Asn Thr Asp Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Ile Tyr Tyr Cys
85 90 95
Val Arg Gly Phe Gly Tyr Ser Tyr Asn Tyr Asp Tyr Tyr Tyr Gly Met
100 105 110
Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 238
<211> 125
<212> PRT
<213> homo sapiens

<400> 238
Gln Val Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
1 5 10 15
Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Asp
20 25 30
Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met Gly
35 40 45
Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe Gln
50 55 60
Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr Met
65 70 75 80
Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95
Arg Glu Gly Ile Ala Val Ala Gly Thr Tyr Tyr Tyr Tyr Tyr Gly Met
100 105 110
Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 239
<211> 126
<212> PRT
<213> homo sapiens

<400> 239
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Thr Tyr
20 25 30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
35 40 45

```
Gly Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe
    50                  55                  60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Leu Ser Thr Ala Tyr
65                  70                  75                  80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Asp Ile Val Val Val Val Ala Ala Thr Asn Tyr Tyr Asn Gly
            100                 105                 110
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

<210> 240
<211> 125
<212> PRT
<213> homo sapiens

<400> 240

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1               5                  10                  15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
Gly Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe
    50                  55                  60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Gly Ser Gly Tyr Ser Tyr Gly Tyr Asp Tyr Tyr Tyr Gly Met
            100                 105                 110
Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

<210> 241
<211> 126
<212> PRT
<213> homo sapiens

<400> 241

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1               5                  10                  15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Ser Tyr
            20                  25                  30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
Gly Trp Met Asn Pro Asn Asn Gly Asn Thr Gly Tyr Ala Gln Lys Phe
    50                  55                  60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Asp Ile Val Val Val Val Thr Ala Thr Asp Tyr Tyr Tyr Gly
            100                 105                 110
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

<210> 242

<211> 127
<212> PRT
<213> homo sapiens

<400> 242
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Met Asn Pro Asn Ser Gly Asp Thr Gly Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys
85 90 95
Ala Arg Met Arg Asp Ile Val Ala Thr Ser Tyr Tyr Tyr Tyr Phe Tyr
100 105 110
Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 243
<211> 127
<212> PRT
<213> homo sapiens

<400> 243
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
50 55 60
Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp His Tyr Tyr Asp Ser Ser Asp Tyr Leu Tyr Tyr Tyr Tyr
100 105 110
Gly Leu Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 244
<211> 69
<212> PRT
<213> homo sapiens

<400> 244
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Gln Gly Thr Leu
50 55 60

Val Thr Val Ser Ser
65

<210> 245
<211> 126
<212> PRT
<213> homo sapiens

<400> 245
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Lys
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Glu Thr Phe Ser Ser Tyr
20 25 30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ala Val Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Gln Gly Tyr Arg Tyr Ala Gly Tyr Tyr Tyr Asp Tyr Gly
100 105 110
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 246
<211> 126
<212> PRT
<213> homo sapiens

<400> 246
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Phe Ser Ser Tyr
20 25 30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ala Asp Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Gln Gly Tyr Ser Tyr Gly Tyr Val Tyr Tyr Asp Tyr Gly
100 105 110
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 247
<211> 126
<212> PRT
<213> homo sapiens

<400> 247
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr

```
           20                  25                  30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
       35                  40                  45
Ala Ile Ile Trp Tyr Asp Gly Asn Asp Lys Tyr Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Val Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
Leu Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95
Arg Gly Tyr Tyr Tyr Asp Ser Ser Asp Tyr Leu Tyr Tyr Tyr Tyr Gly
            100                 105                 110
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

<210> 248
<211> 126
<212> PRT
<213> homo sapiens

<400> 248

```
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
 1               5                  10                  15
Ser Leu Lys Ile Ser Cys Glu Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
            20                  25                  30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
    50                  55                  60
Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95
Ala Arg His Val Ser Tyr Tyr Tyr Val Ser Gly Ser Tyr Tyr Asn Val
            100                 105                 110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120                 125
```

<210> 249
<211> 126
<212> PRT
<213> homo sapiens

<400> 249

```
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
 1               5                  10                  15
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Arg Phe Thr Ser Tyr
            20                  25                  30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
    50                  55                  60
Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95
Ala Arg His Gly Ser Tyr Tyr Tyr Gly Ser Glu Thr Tyr Tyr Asn Val
            100                 105                 110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120                 125
```

<210> 250
<211> 129
<212> PRT
<213> homo sapiens

<400> 250
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
50 55 60
Gln Gly Gln Ala Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95
Ala Arg His Val Asp Val Gly Ala Thr Ile Gly Gly Tyr Tyr Tyr Tyr
100 105 110
Tyr His Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser
115 120 125
Ser

<210> 251
<211> 126
<212> PRT
<213> homo sapiens

<400> 251
Glu Val Gln Leu Val Gln Ser Gly Thr Glu Val Lys Lys Pro Gly Glu
1 5 10 15
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Arg Phe Thr Ser Tyr
20 25 30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
50 55 60
Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95
Ala Arg His Gly Ser Tyr Tyr Tyr Asn Ser Gly Ser Tyr Tyr Asn Val
100 105 110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 252
<211> 127
<212> PRT
<213> homo sapiens

<400> 252
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr

```
           20                  25                  30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Ala Lys Tyr Ser Pro Ser Phe
    50                  55                  60
Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Ala Thr Ala Met Tyr Tyr
                85                  90                  95
Cys Ala Arg His Tyr Asp Tyr Val Trp Arg Asn Tyr Arg Tyr Thr Gly
            100                 105                 110
Trp Phe Asp Pro Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120                 125
```

<210> 253
<211> 111
<212> PRT
<213> homo sapiens

<400> 253

```
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
 1               5                  10                  15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
            20                  25                  30
Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Leu Lys Pro Gly Gln Ser
        35                  40                  45
Pro Gln Leu Leu Ile Tyr Leu Gly Ser Ser Arg Ala Ser Gly Val Pro
    50                  55                  60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Thr
                85                  90                  95
Leu Gln Thr Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
            100                 105                 110
```

<210> 254
<211> 111
<212> PRT
<213> homo sapiens

<400> 254

```
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
 1               5                  10                  15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu Gln Ser
            20                  25                  30
Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45
Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
    50                  55                  60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
                85                  90                  95
Leu Gln Thr Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105                 110
```

<210> 255
<211> 113

<212> PRT
<213> homo sapiens

<400> 255
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
20 25 30
Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45
Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80
Ser Arg Val Glu Ala Asp Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
85 90 95
Leu Gln Ser Leu Met Cys Ser Phe Gly Gln Gly Thr Lys Leu Glu Ile
100 105 110
Lys

<210> 256
<211> 107
<212> PRT
<213> homo sapiens

<400> 256
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Asn Cys Arg Ala Ser Gln Gly Ile Ser Asn Asp
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile
35 40 45
Tyr Ala Ala Ser Thr Leu Gln Leu Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Val Ala Thr Tyr Tyr Cys Gln Lys Tyr Asn Ser Ala Pro Phe
85 90 95
Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
100 105

<210> 257
<211> 107
<212> PRT
<213> homo sapiens

<400> 257
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Asn Tyr
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile
35 40 45
Tyr Ala Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Val Ala Thr Tyr Tyr Cys Gln Lys Tyr Asn Ser Ala Pro Leu

```
                85                  90                  95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105
```

<210> 258
<211> 107
<212> PRT
<213> homo sapiens

<400> 258
```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Asn Tyr
            20                  25                  30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Asn Leu Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Ser Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Val Ala Ala Tyr Tyr Cys Gln Lys Cys Asn Ser Ala Pro Trp
                85                  90                  95
Thr Phe Gly Gln Gly Thr Thr Val Glu Ile Lys
            100                 105
```

<210> 259
<211> 108
<212> PRT
<213> homo sapiens

<400> 259
```
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
 1               5                  10                  15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
            20                  25                  30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35                  40                  45
Ile Tyr Ala Thr Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    50                  55                  60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65                  70                  75                  80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
                85                  90                  95
Cys Ser Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105
```

<210> 260
<211> 108
<212> PRT
<213> homo sapiens

<400> 260
```
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
 1               5                  10                  15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
            20                  25                  30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35                  40                  45
```

```
Ile Tyr Gly Ala Ser Asn Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    50                  55                  60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65                  70                  75                  80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Leu
                85                  90                  95
Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
            100                 105
```

<210> 261
<211> 107
<212> PRT
<213> homo sapiens

<400> 261
```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
            20                  25                  30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Asp Pro Cys
                85                  90                  95
Ser Phe Gly Gln Gly Thr Lys Leu Glu Ile Arg
            100                 105
```

<210> 262
<211> 107
<212> PRT
<213> homo sapiens

<400> 262
```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
            20                  25                  30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Asp Pro Cys
                85                  90                  95
Ser Phe Gly Gln Gly Thr Lys Leu Glu Ile Arg
            100                 105
```

<210> 263
<211> 107
<212> PRT
<213> homo sapiens

<400> 263
```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
```

```
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
            20                  25                  30
Leu Gly Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Leu
                85                  90                  95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105
```

<210> 264
<211> 107
<212> PRT
<213> homo sapiens

<400> 264

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
            20                  25                  30
Leu Gly Trp Tyr Gln Gln Ile Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Ser Leu Gln Arg Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Trp
                85                  90                  95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105
```

<210> 265
<211> 107
<212> PRT
<213> homo sapiens

<400> 265

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
            20                  25                  30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Trp
                85                  90                  95
Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105
```

<210> 266
<211> 107

<212> PRT
<213> homo sapiens

<400> 266
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
20 25 30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Trp
85 90 95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 267
<211> 107
<212> PRT
<213> homo sapiens

<400> 267
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
20 25 30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Leu
85 90 95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 268
<211> 107
<212> PRT
<213> homo sapiens

<400> 268
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
20 25 30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Trp
85 90 95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys

100 105

<210> 269
<211> 107
<212> PRT
<213> homo sapiens

<400> 269
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
20 25 30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45
Phe Ala Ala Ser Ser Leu Pro Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Ser Gly Tyr Pro Pro
85 90 95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 270
<211> 126
<212> PRT
<213> homo sapiens

<400> 270
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Phe Arg Thr Tyr
20 25 30
Asn Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Ser Ile Ser Ser Ser Ser Ser Asn Ile Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Ile Met Ile Thr Phe Gly Gly Ile Ile Ala Ser Phe Tyr
100 105 110
Phe Asp Tyr Trp Gly Gln Gly Thr Val Leu Thr Val Ser Ser
115 120 125

<210> 271
<211> 98
<212> PRT
<213> homo sapiens

<400> 271
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30
Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

```
Ser Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg
```

<210> 272
<211> 98
<212> PRT
<213> homo sapiens

<220>
<221> VARIANT
<222> 28, 30, 33, 57
<223> Xaa = Any Amino Acid

<221> VARIANT
<222> 28, 30, 33, 57
<223> Xaa = Any Amino Acid

<400> 272

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
 1               5                  10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Xaa Phe Xaa Ser Tyr
            20                  25                  30
Xaa Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ser Ser Ile Ser Ser Ser Ser Ser Xaa Ile Tyr Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg
```

<210> 273
<211> 108
<212> PRT
<213> homo sapiens

<400> 273

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asp Asn
            20                  25                  30
Asp Leu Gly Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu
        35                  40                  45
Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser
    50                  55                  60
Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln
65                  70                  75                  80
Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro
                85                  90                  95
Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105
```

<210> 274
<211> 96
<212> PRT
<213> homo sapiens

<400> 274
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asp Asn
20 25 30
Asp Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu
35 40 45
Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser
50 55 60
Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln
65 70 75 80
Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro
85 90 95

<210> 275
<211> 96
<212> PRT
<213> homo sapiens

<400> 275
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asp Asn
20 25 30
Asp Leu Gly Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu
35 40 45
Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser
50 55 60
Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln
65 70 75 80
Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro
85 90 95

<210> 276
<211> 120
<212> PRT
<213> homo sapiens

<400> 276
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Ile Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Val Ser Ser Asn
20 25 30
Tyr Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Val Ile Tyr Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
50 55 60
Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu
65 70 75 80
Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95
Gly Thr Val Thr Thr Asn Tyr Tyr Tyr Gly Met Asp Val Trp Gly Gln

100 105 110
Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 277
<211> 97
<212> PRT
<213> homo sapiens

<400> 277
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Ile Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Val Ser Ser Asn
20 25 30
Tyr Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Val Ile Tyr Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
50 55 60
Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu
65 70 75 80
Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95
Arg

<210> 278
<211> 96
<212> PRT
<213> homo sapiens

<400> 278
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Ile Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Val Ser Ser Asn
20 25 30
Tyr Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Val Ile Tyr Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
50 55 60
Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu
65 70 75 80
Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

<210> 279
<211> 111
<212> PRT
<213> homo sapiens

<400> 279
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu Gln Ser
20 25 30
Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45
Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60

```
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
                85                  90                  95
Leu Gln Thr Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105                 110


<210> 280
<211> 100
<212> PRT
<213> homo sapiens

<400> 280
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
 1               5                  10                  15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
            20                  25                  30
Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45
Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
    50                  55                  60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
                85                  90                  95
Leu Gln Thr Pro
            100


<210> 281
<211> 99
<212> PRT
<213> homo sapiens

<220>
<221> VARIANT
<222> 31
<223> Xaa = Any Amino Acid

<221> VARIANT
<222> 31
<223> Xaa = Any Amino Acid

<400> 281
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
 1               5                  10                  15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu Xaa Ser
            20                  25                  30
Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45
Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
    50                  55                  60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
                85                  90                  95
Leu Gln Thr
```

<210> 282
<211> 126
<212> PRT
<213> homo sapiens

<400> 282
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Lys
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ala Val Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Gln Gly Tyr Arg Tyr Ala Gly Tyr Tyr Tyr Asp Tyr Gly
100 105 110
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 283
<211> 98
<212> PRT
<213> homo sapiens

<400> 283
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ala Val Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg

<210> 284
<211> 98
<212> PRT
<213> homo sapiens

<400> 284
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Lys
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ala Val Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr

65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg

<210> 285
<211> 107
<212> PRT
<213> homo sapiens

<400> 285
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
20 25 30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Leu
85 90 95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 286
<211> 95
<212> PRT
<213> homo sapiens

<400> 286
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
20 25 30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro
85 90 95

<210> 287
<211> 95
<212> PRT
<213> homo sapiens

<400> 287
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
20 25 30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro
85 90 95

<210> 288
<211> 126
<212> PRT
<213> homo sapiens

<400> 288
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Glu Gly Ile Ala Val Ala Gly Thr Tyr Tyr Tyr Tyr Tyr Gly
100 105 110
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 289
<211> 98
<212> PRT
<213> homo sapiens

<400> 289
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg

<210> 290
<211> 98
<212> PRT
<213> homo sapiens

<400> 290
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala

```
 1               5                  10                  15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
Gly Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe
    50                  55                  60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg
```

<210> 291
<211> 107
<212> PRT
<213> homo sapiens

<400> 291

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
            20                  25                  30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Phe Cys Leu Gln His Asn Ser Tyr Pro Phe
                85                  90                  95
Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
            100                 105
```

<210> 292
<211> 95
<212> PRT
<213> homo sapiens

<400> 292

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
            20                  25                  30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro
                85                  90                  95
```

<210> 293
<211> 95
<212> PRT
<213> homo sapiens

<400> 293
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
20 25 30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Phe Cys Leu Gln His Asn Ser Tyr Pro
85 90 95

<210> 294
<211> 126
<212> PRT
<213> homo sapiens

<400> 294
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Val Met Ile Thr Phe Gly Gly Val Ile Val His Tyr Gly
100 105 110
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 295
<211> 98
<212> PRT
<213> homo sapiens

<400> 295
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg

<210> 296
<211> 98
<212> PRT
<213> homo sapiens

<400> 296
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg

<210> 297
<211> 107
<212> PRT
<213> homo sapiens

<400> 297
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
20 25 30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Asp Pro Cys
85 90 95
Ser Phe Gly Gln Gly Thr Lys Leu Glu Ile Arg
100 105

<210> 298
<211> 95
<212> PRT
<213> homo sapiens

<400> 298
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
20 25 30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

```
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro
                85                  90                  95


<210> 299
<211> 95
<212> PRT
<213> homo sapiens

<220>
<221> VARIANT
<222> 94
<223> Xaa = Any Amino Acid

<221> VARIANT
<222> 94
<223> Xaa = Any Amino Acid

<400> 299
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
            20                  25                  30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Xaa Pro
                85                  90                  95


<210> 300
<211> 126
<212> PRT
<213> homo sapiens

<400> 300
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
 1               5                  10                  15
Ser Leu Lys Ile Ser Cys Glu Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
            20                  25                  30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
    50                  55                  60
Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95
Ala Arg His Val Ser Tyr Tyr Tyr Val Ser Gly Ser Tyr Tyr Asn Val
            100                 105                 110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120                 125


<210> 301
<211> 98
<212> PRT
<213> homo sapiens
```

<400> 301
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
50 55 60
Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95
Ala Arg

<210> 302
<211> 98
<212> PRT
<213> homo sapiens

<220>
<221> VARIANT
<222> 23
<223> Xaa = Any Amino Acid

<221> VARIANT
<222> 23
<223> Xaa = Any Amino Acid

<400> 302
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15
Ser Leu Lys Ile Ser Cys Xaa Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
50 55 60
Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95
Ala Arg

<210> 303
<211> 107
<212> PRT
<213> homo sapiens

<400> 303
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
20 25 30
Leu Gly Trp Tyr Gln Gln Ile Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45

```
Tyr Ala Ala Ser Ser Leu Gln Arg Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Trp
                85                  90                  95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105


<210> 304
<211> 95
<212> PRT
<213> homo sapiens

<400> 304
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
            20                  25                  30
Leu Gly Trp Tyr Gln Gln Ile Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro
                85                  90                  95


<210> 305
<211> 95
<212> PRT
<213> homo sapiens

<220>
<221> VARIANT
<222> 56
<223> Xaa = Any Amino Acid

<221> VARIANT
<222> 56
<223> Xaa = Any Amino Acid

<400> 305
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
            20                  25                  30
Leu Gly Trp Tyr Gln Gln Ile Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Ser Leu Gln Xaa Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro
                85                  90                  95


<210> 306
<211> 126
```

<212> PRT
<213> homo sapiens

<400> 306
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Phe Ser Ser Tyr
20 25 30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ala Asp Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Gln Gly Tyr Ser Tyr Gly Tyr Val Tyr Tyr Asp Tyr Gly
100 105 110
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 307
<211> 98
<212> PRT
<213> homo sapiens

<400> 307
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ala Asp Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg

<210> 308
<211> 98
<212> PRT
<213> homo sapiens

<400> 308
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Phe Ser Ser Tyr
20 25 30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ala Asp Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys

85 90 95

Ala Arg

<210> 309
<211> 107
<212> PRT
<213> homo sapiens

<400> 309
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asp Asn
20 25 30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Trp
85 90 95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 310
<211> 95
<212> PRT
<213> homo sapiens

<400> 310
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asp Asn
20 25 30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro
85 90 95

<210> 311
<211> 95
<212> PRT
<213> homo sapiens

<400> 311
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asp Asn
20 25 30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

```
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro
                85                  90                  95


<210> 312
<211> 98
<212> PRT
<213> homo sapiens

<400> 312
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
 1               5                  10                  15
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
            20                  25                  30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
    50                  55                  60
Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95
Ala Arg


<210> 313
<211> 126
<212> PRT
<213> homo sapiens

<400> 313
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
 1               5                  10                  15
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
            20                  25                  30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
    50                  55                  60
Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95
Ala Arg His Gly Ser Tyr Tyr Tyr Gly Ser Glu Thr Tyr Tyr Asn Val
            100                 105                 110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120                 125


<210> 314
<211> 98
<212> PRT
<213> homo sapiens

<220>
<221> VARIANT
<222> 28
<223> Xaa = Any Amino Acid
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<221> VARIANT
<222> 28
<223> Xaa = Any Amino Acid

<400> 314
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Xaa Phe Thr Ser Tyr
20 25 30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
50 55 60
Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95
Ala Arg

<210> 315
<211> 95
<212> PRT
<213> homo sapiens

<400> 315
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
20 25 30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro
85 90 95

<210> 316
<211> 107
<212> PRT
<213> homo sapiens

<400> 316
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
20 25 30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Trp
85 90 95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys

100 105

<210> 317
<211> 95
<212> PRT
<213> homo sapiens

<400> 317
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
20 25 30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro
85 90 95

<210> 318
<211> 98
<212> PRT
<213> homo sapiens

<400> 318
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
50 55 60
Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95
Ala Arg

<210> 319
<211> 129
<212> PRT
<213> homo sapiens

<400> 319
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
50 55 60
Gln Gly Gln Ala Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

```
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95
Ala Arg His Val Asp Val Gly Ala Thr Ile Gly Gly Tyr Tyr Tyr Tyr
            100                 105                 110
Tyr His Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser
        115                 120                 125
Ser
```

<210> 320
<211> 98
<212> PRT
<213> homo sapiens

<220>
<221> VARIANT
<222> 68
<223> Xaa = Any Amino Acid

<221> VARIANT
<222> 68
<223> Xaa = Any Amino Acid

<400> 320

```
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
 1               5                  10                  15
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
            20                  25                  30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
    50                  55                  60
Gln Gly Gln Xaa Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95
Ala Arg
```

<210> 321
<211> 100
<212> PRT
<213> homo sapiens

<400> 321

```
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
 1               5                  10                  15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
            20                  25                  30
Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45
Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
    50                  55                  60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
                85                  90                  95
Leu Gln Thr Pro
            100
```

<210> 322
<211> 114
<212> PRT
<213> homo sapiens

<400> 322
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
20 25 30
Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45
Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80
Ser Arg Val Glu Ala Asp Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
85 90 95
Leu Gln Thr Pro Leu Met Cys Ser Phe Gly Gln Gly Thr Lys Leu Glu
100 105 110
Ile Lys

<210> 323
<211> 99
<212> PRT
<213> homo sapiens

<400> 323
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
20 25 30
Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45
Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
85 90 95
Leu Gln Ser

<210> 324
<211> 98
<212> PRT
<213> homo sapiens

<400> 324
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu

```
    50                  55                  60
Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg
```

<210> 325
<211> 127
<212> PRT
<213> homo sapiens

<400> 325

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1               5                  10                  15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30
Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
    50                  55                  60
Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Asp His Tyr Tyr Asp Ser Ser Asp Tyr Leu Tyr Tyr Tyr Tyr
            100                 105                 110
Gly Leu Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

<210> 326
<211> 98
<212> PRT
<213> homo sapiens

<400> 326

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1               5                  10                  15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30
Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
    50                  55                  60
Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg
```

<210> 327
<211> 96
<212> PRT
<213> homo sapiens

<400> 327

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Phe Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Asn
            20                  25                  30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu
        35                  40                  45
Ile Tyr Ala Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser
    50                  55                  60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln
65                  70                  75                  80
Pro Glu Asp Val Ala Thr Tyr Tyr Cys Gln Lys Tyr Asn Ser Ala Pro
                85                  90                  95
```

<210> 328
<211> 108
<212> PRT
<213> homo sapiens

<400> 328

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Phe Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Asn
            20                  25                  30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu
        35                  40                  45
Ile Tyr Ala Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser
    50                  55                  60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln
65                  70                  75                  80
Pro Glu Asp Val Ala Thr Tyr Tyr Cys Gln Lys Tyr Asn Ser Ala Pro
                85                  90                  95
Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105
```

<210> 329
<211> 96
<212> PRT
<213> homo sapiens

<400> 329

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Phe Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Asn
            20                  25                  30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu
        35                  40                  45
Ile Tyr Ala Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser
    50                  55                  60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln
65                  70                  75                  80
Pro Glu Asp Val Ala Thr Tyr Tyr Cys Gln Lys Tyr Asn Ser Ala Pro
                85                  90                  95
```

<210> 330
<211> 98
<212> PRT
<213> homo sapiens

<400> 330
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ala Val Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg

<210> 331
<211> 127
<212> PRT
<213> homo sapiens

<400> 331
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ala Ile Ile Trp Tyr Asp Gly Asn Asp Lys Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Val Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Gly Tyr Tyr Tyr Asp Ser Ser Asp Tyr Leu Tyr Tyr Tyr Tyr
100 105 110
Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 332
<211> 98
<212> PRT
<213> homo sapiens

<220>
<221> VARIANT
<222> 56, 57
<223> Xaa = Any Amino Acid

<221> VARIANT
<222> 56, 57
<223> Xaa = Any Amino Acid

<400> 332
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val

```
        35                  40                  45
Ala Ile Ile Trp Tyr Asp Gly Xaa Xaa Lys Tyr Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg
```

<210> 333
<211> 95
<212> PRT
<213> homo sapiens

<400> 333

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Asn Tyr
            20                  25                  30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Val Ala Thr Tyr Tyr Cys Gln Lys Tyr Asn Ser Ala Pro
                85                  90                  95
```

<210> 334
<211> 107
<212> PRT
<213> homo sapiens

<400> 334

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Asn Tyr
            20                  25                  30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Asn Leu Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Ser Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Val Ala Ala Tyr Tyr Cys Gln Lys Cys Asn Ser Ala Pro Trp
                85                  90                  95
Thr Phe Gly Gln Gly Thr Thr Val Glu Ile Lys
            100                 105
```

<210> 335
<211> 95
<212> PRT
<213> homo sapiens

<220>
<221> VARIANT
<222> 45, 85, 91

<223> Xaa = Any Amino Acid

<221> VARIANT
<222> 45, 85, 91
<223> Xaa = Any Amino Acid

<400> 335
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Asn Tyr
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Xaa Leu Leu Ile
35 40 45
Tyr Ala Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Val Ala Xaa Tyr Tyr Cys Gln Lys Xaa Asn Ser Ala Pro
85 90 95

<210> 336
<211> 98
<212> PRT
<213> homo sapiens

<400> 336
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
50 55 60
Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95
Ala Arg

<210> 337
<211> 126
<212> PRT
<213> homo sapiens

<400> 337
Glu Val Gln Leu Val Gln Ser Gly Thr Glu Val Lys Lys Pro Gly Glu
1 5 10 15
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Arg Phe Thr Ser Tyr
20 25 30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
50 55 60
Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

```
Ala Arg His Gly Ser Tyr Tyr Tyr Asn Ser Gly Ser Tyr Tyr Asn Val
           100                 105                 110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120                 125


<210> 338
<211> 98
<212> PRT
<213> homo sapiens

<220>
<221> VARIANT
<222> 9, 28
<223> Xaa = Any Amino Acid

<221> VARIANT
<222> 9, 28
<223> Xaa = Any Amino Acid

<400> 338
Glu Val Gln Leu Val Gln Ser Gly Xaa Glu Val Lys Lys Pro Gly Glu
 1               5                  10                  15
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Xaa Phe Thr Ser Tyr
            20                  25                  30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
    50                  55                  60
Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95
Ala Arg


<210> 339
<211> 95
<212> PRT
<213> homo sapiens

<400> 339
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
            20                  25                  30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro
                85                  90                  95


<210> 340
<211> 107
<212> PRT
<213> homo sapiens
```

<400> 340
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
20 25 30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Trp
85 90 95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 341
<211> 95
<212> PRT
<213> homo sapiens

<400> 341
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
20 25 30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro
85 90 95

<210> 342
<211> 98
<212> PRT
<213> homo sapiens

<400> 342
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg

<210> 343

<211> 125
<212> PRT
<213> homo sapiens

<400> 343
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Gly Ser Gly Tyr Ser Tyr Gly Tyr Asp Tyr Tyr Tyr Gly Met
100 105 110
Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 344
<211> 98
<212> PRT
<213> homo sapiens

<400> 344
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg

<210> 345
<211> 95
<212> PRT
<213> homo sapiens

<400> 345
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Asn Tyr
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile
35 40 45
Tyr Ala Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

```
Glu Asp Val Ala Thr Tyr Tyr Cys Gln Lys Tyr Asn Ser Ala Pro
                85                  90                  95


<210> 346
<211> 107
<212> PRT
<213> homo sapiens

<400> 346
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Asn Cys Arg Ala Ser Gln Gly Ile Ser Asn Asp
            20                  25                  30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Val Ala Thr Tyr Tyr Cys Gln Lys Tyr Asn Ser Ala Pro Phe
                85                  90                  95
Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
            100                 105


<210> 347
<211> 95
<212> PRT
<213> homo sapiens

<220>
<221> VARIANT
<222> 22, 32, 56
<223> Xaa = Any Amino Acid

<221> VARIANT
<222> 22, 32, 56
<223> Xaa = Any Amino Acid

<400> 347
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Xaa Cys Arg Ala Ser Gln Gly Ile Ser Asn Xaa
            20                  25                  30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Thr Leu Gln Xaa Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Val Ala Thr Tyr Tyr Cys Gln Lys Tyr Asn Ser Ala Pro
                85                  90                  95


<210> 348
<211> 98
<212> PRT
<213> homo sapiens

<400> 348
```

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1               5                  10                  15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
Gly Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe
    50                  55                  60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg
```

<210> 349
<211> 126
<212> PRT
<213> homo sapiens

<400> 349

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1               5                  10                  15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Ser Tyr
            20                  25                  30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
Gly Trp Met Asn Pro Asn Asn Gly Asn Thr Gly Tyr Ala Gln Lys Phe
    50                  55                  60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Asp Ile Val Val Val Val Thr Ala Thr Asp Tyr Tyr Tyr Gly
            100                 105                 110
Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

<210> 350
<211> 98
<212> PRT
<213> homo sapiens

<220>
<221> VARIANT
<222> 55
<223> Xaa = Any Amino Acid

<221> VARIANT
<222> 55
<223> Xaa = Any Amino Acid

<400> 350

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1               5                  10                  15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
```

```
Gly Trp Met Asn Pro Asn Xaa Gly Asn Thr Gly Tyr Ala Gln Lys Phe
    50                  55                  60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg
```

<210> 351
<211> 95
<212> PRT
<213> homo sapiens

<400> 351

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1                  5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
            20                  25                  30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro
                85                  90                  95
```

<210> 352
<211> 107
<212> PRT
<213> homo sapiens

<400> 352

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1                  5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
            20                  25                  30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
        35                  40                  45
Phe Ala Ala Ser Ser Leu Pro Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Ser Gly Tyr Pro Pro
                85                  90                  95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105
```

<210> 353
<211> 95
<212> PRT
<213> homo sapiens

<220>
<221> VARIANT
<222> 55, 92, 93
<223> Xaa = Any Amino Acid

<221> VARIANT
<222> 55, 92, 93
<223> Xaa = Any Amino Acid

<400> 353
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
20 25 30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45
Tyr Ala Ala Ser Ser Leu Xaa Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Xaa Xaa Tyr Pro
85 90 95

<210> 354
<211> 126
<212> PRT
<213> homo sapiens

<400> 354
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
50 55 60
Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Val Glu Tyr Tyr Tyr Asp Gly Ser Gly Tyr Tyr Tyr Tyr
100 105 110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 355
<211> 98
<212> PRT
<213> homo sapiens

<400> 355
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
50 55 60
Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys

```
                85                  90                  95
Ala Arg


<210> 356
<211> 98
<212> PRT
<213> homo sapiens

<400> 356
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1               5                  10                  15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30
Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
    50                  55                  60
Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg


<210> 357
<211> 108
<212> PRT
<213> homo sapiens

<400> 357
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp
            20                  25                  30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Ile Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Ser Tyr Tyr Cys Gln Gln Ser Asn Ser Phe Pro Arg
                85                  90                  95
Phe Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105


<210> 358
<211> 95
<212> PRT
<213> homo sapiens

<400> 358
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp
            20                  25                  30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45
```

```
Tyr Ala Ala Ser Ile Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Ser Phe Pro
                85                  90                  95


<210> 359
<211> 95
<212> PRT
<213> homo sapiens

<220>
<221> VARIANT
<222> 53
<223> Xaa = Any Amino Acid

<221> VARIANT
<222> 53
<223> Xaa = Any Amino Acid

<400> 359
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
 1               5                  10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp
            20                  25                  30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45
Tyr Ala Ala Ser Xaa Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Ser Tyr Tyr Cys Gln Gln Ser Asn Ser Phe Pro
                85                  90                  95


<210> 360
<211> 127
<212> PRT
<213> homo sapiens

<400> 360
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1               5                  10                  15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
Gly Trp Met Asn Pro Asn Ser Gly Asp Thr Gly Tyr Ala Gln Lys Phe
    50                  55                  60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys
                85                  90                  95
Ala Arg Met Arg Asp Ile Val Ala Thr Ser Tyr Tyr Tyr Tyr Phe Tyr
            100                 105                 110
Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125
```

<210> 361
<211> 98
<212> PRT
<213> homo sapiens

<400> 361
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Met Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg

<210> 362
<211> 98
<212> PRT
<213> homo sapiens

<220>
<221> VARIANT
<222> 57
<223> Xaa = Any Amino Acid

<221> VARIANT
<222> 57
<223> Xaa = Any Amino Acid

<400> 362
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Met Asn Pro Asn Ser Gly Xaa Thr Gly Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys
85 90 95
Ala Arg

<210> 363
<211> 111
<212> PRT
<213> homo sapiens

<400> 363
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

```
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
            20                  25                  30
Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Leu Lys Pro Gly Gln Ser
        35                  40                  45
Pro Gln Leu Leu Ile Tyr Leu Gly Ser Ser Arg Ala Ser Gly Val Pro
    50                  55                  60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Thr
                85                  90                  95
Leu Gln Thr Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
            100                 105                 110


<210> 364
<211> 100
<212> PRT
<213> homo sapiens

<400> 364
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
 1               5                  10                  15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
            20                  25                  30
Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Leu Lys Pro Gly Gln Ser
        35                  40                  45
Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
    50                  55                  60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
                85                  90                  95
Leu Gln Thr Pro
            100


<210> 365
<211> 99
<212> PRT
<213> homo sapiens

<220>
<221> VARIANT
<222> 43, 58, 96
<223> Xaa = Any Amino Acid

<221> VARIANT
<222> 43, 58, 96
<223> Xaa = Any Amino Acid

<400> 365
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
 1               5                  10                  15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
            20                  25                  30
Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Xaa Lys Pro Gly Gln Ser
        35                  40                  45
Pro Gln Leu Leu Ile Tyr Leu Gly Ser Xaa Arg Ala Ser Gly Val Pro
    50                  55                  60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80
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Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Xaa
85 90 95
Leu Gln Thr

<210> 366
<211> 126
<212> PRT
<213> homo sapiens

<400> 366
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Ala Lys Tyr Ser Pro Ser Phe
50 55 60
Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95
Ala Arg His Tyr Asp Tyr Val Trp Arg Asn Tyr Arg Tyr Thr Gly Trp
100 105 110
Phe Asp Pro Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 367
<211> 98
<212> PRT
<213> homo sapiens

<400> 367
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
50 55 60
Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95
Ala Arg

<210> 368
<211> 98
<212> PRT
<213> homo sapiens

<220>
<221> VARIANT
<222> 58
<223> Xaa = Any Amino Acid

<221> VARIANT
<222> 58
<223> Xaa = Any Amino Acid

<400> 368
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15
Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30
Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45
Gly Ile Ile Tyr Pro Gly Asp Ser Asp Xaa Lys Tyr Ser Pro Ser Phe
50 55 60
Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95
Ala Arg

<210> 369
<211> 108
<212> PRT
<213> homo sapiens

<400> 369
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45
Ile Tyr Gly Ala Ser Asn Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Leu
85 90 95
Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
100 105

<210> 370
<211> 96
<212> PRT
<213> homo sapiens

<400> 370
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45
Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro

85 90 95

<210> 371
<211> 95
<212> PRT
<213> homo sapiens

<220>
<221> VARIANT
<222> 54
<223> Xaa = Any Amino Acid

<221> VARIANT
<222> 54
<223> Xaa = Any Amino Acid

<400> 371
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45
Ile Tyr Gly Ala Ser Xaa Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser
85 90 95

<210> 372
<211> 125
<212> PRT
<213> homo sapiens

<400> 372
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Ile Asn Pro Asn Ser Gly Asn Thr Asp Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Ile Tyr Tyr Cys
85 90 95
Val Arg Gly Phe Gly Tyr Ser Tyr Asn Tyr Asp Tyr Tyr Tyr Gly Met
100 105 110
Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 373
<211> 98
<212> PRT
<213> homo sapiens

<400> 373
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Met Asn Pro Asn Ser Gly Asn Thr Asp Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg

<210> 374
<211> 98
<212> PRT
<213> homo sapiens

<220>
<221> VARIANT
<222> 59, 73, 97
<223> Xaa = Any Amino Acid

<221> VARIANT
<222> 59, 73, 97
<223> Xaa = Any Amino Acid

<400> 374
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Ile Asn Pro Asn Ser Gly Asn Thr Xaa Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Xaa Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Ile Tyr Tyr Cys
85 90 95
Xaa Arg

<210> 375
<211> 108
<212> PRT
<213> homo sapiens

<400> 375
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45
Ile Tyr Ala Thr Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser

```
    50                  55                  60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65                  70                  75                  80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
                85                  90                  95
Cys Ser Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105
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<210> 376
<211> 96
<212> PRT
<213> homo sapiens

<400> 376

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Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
 1               5                  10                  15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
            20                  25                  30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35                  40                  45
Ile Tyr Gly Thr Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    50                  55                  60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65                  70                  75                  80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
                85                  90                  95
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<210> 377
<211> 96
<212> PRT
<213> homo sapiens

<400> 377

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Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
 1               5                  10                  15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
            20                  25                  30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
        35                  40                  45
Ile Tyr Ala Thr Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
    50                  55                  60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65                  70                  75                  80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
                85                  90                  95
```